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The Rockefeller University

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news & notes

THE NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

FRIDAY LECTURE

Nathans to discuss Frizzled receptors today

Jeremy Nathans, a professor at Johns Hopkins University School of Medicine and an investigator at the Howard Hughes Medical Institute, will present the Friday lecture today (March 23). His topic will be "The Frizzled Family of Cell Surface Receptors."

"Understanding the development and function of the human nervous system is the single greatest challenge facing modern biology," Nathans says. The broad range of questions that can be asked within this arena invites a corresponding breadth of experimental approaches, ranging from structural chemistry to psychology. His laboratory uses molecular biological methods to discover and characterize novel genes and proteins that control neuronal development and function. He has made landmark contributions to the current understanding of the structure and function of visual photoreceptors and of the molecular genetics of color vision in humans.

During the past several years, Nathans has focused on a new family of cell surface receptors that receive organizing information during nervous system development and are homologous to the *Drosophila* tissue polarity gene *frizzled*. The Frizzled receptor protein has a large extracellular amino-terminal domain followed by seven predicted transmembrane segments. The impetus for working on mammalian *frizzled* genes came from observations made during large-scale sequencing of retina-derived cDNA clones. Thus far Nathans has identified novel *frizzled* family members in mammals, zebrafish and several other species.

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Levine receives first Albany Medical Center Prize

President Arnold J. Levine is the first recipient of the Albany Medical Center Prize in Medicine and Biomedical Research. The announcement was made last Wed., March 14, at a news conference at the New York Academy of Sciences. Levine is recognized for his discoveries about the p53 tumor suppressor protein, one of the body's most important defenses against many forms of cancer.

The Albany Medical Center Prize in Medicine and Biomedical Research, which carries a \$500,000 award, is the largest annual prize in science or medicine offered in the United States. The prize honors a physician or scientist whose work has led to significant advances in health care and scientific research.

"The award recognizes Dr. Levine's seminal findings, his ongoing research on p53 and its promise of unlocking the mysteries of cancer," said James J. Barba, president and chief executive officer of the Albany Medical Center, in announcing the prize.

"Dr. Levine, I believe, is going to show us the light at the end of the tunnel," said New York City philanthropist Morris "Marty" Silverman during the news conference. Silverman, who was born in Troy, N.Y., and educated in nearby Albany, established the prize in November 2000 with a \$50 million gift commitment.

Levine, who is the Robert and Harriet Heilbrunn Professor of Cancer Biology, first isolated the p53 protein in 1979 from a monkey virus called SV40. P53

originally was thought to be an oncogene, or tumor accelerator, but Levine and his colleagues later showed that it is, in fact, a tumor suppressor—it prevents cancer. Other scientists went on to show that a mutation in p53 is the single most common genetic change in human cancers, including those of the breast, lung, colon, prostate, bladder and cervix (see story, page 3).

Levine thanked Silverman and the Albany Medical Center Prize committee for the award, emphasizing that his work was made possible by the support of his wife, Linda, his two daughters, and the work of many postdoctoral researchers and graduate students over the course of more than 30 years of research.

Levine plans to donate the



Left to right: Philanthropist Morris Silverman, Rockefeller University President Arnold J. Levine and James J. Barba, president and chief executive officer of the Albany Medical Center.

prize money to four causes: the establishment of a graduate fellowship for minority students at Rockefeller, the Churchill School for Learning Disabled Children, Ballet Hispanico and a college fund for his two-month-old grandson.

"The award will help the things we care a lot about," said Levine.

Schreiber to give Furlaud Lecture on April 6

Rockefeller University Trustee Stuart L. Schreiber, a professor at Harvard University, will present the Richard M. Furlaud Distinguished Lecture on Fri., April 6. His topic will be "Toward a Chemical Genetics."

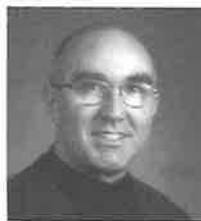
Genetics has been a primary contributor to the understanding of biology. Both forward and reverse genetics rely upon mutant alleles to gain insights into pathways or processes of

interest. Small molecules have also been used to gain insights into biology in ways that are analogous to either forward or reverse genetics. Many of these advances (for example, Arvid Carlsson's use of chlorpromazine to explore the dopamine receptor and Gary Borisy's use of colchicine to discover tubulin) have been brought to light on a case-by-case basis. In his lecture, Schreiber will discuss research

aimed at the development of chemical genetics, where small molecules are used in a systematic way to explore biology.

Schreiber is an investigator at the Howard Hughes Medical Institute and a Morris Loeb Professor at Harvard University, where he is a member of the Department of Chemistry and

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Stuart Schreiber, a Rockefeller University trustee, is a Morris Loeb Professor at Harvard University and an investigator at the Howard Hughes Medical Institute.

Women&Science forum focuses on biotechnology

On Thurs., March 15, The Rockefeller University's *Women&Science* initiative held its seventh in a series of breakfast forums for an audience of 200. In a departure from previous programs focusing on women's health issues, this program featured presentations by prominent women speaking on "Biotechnology in the Post-Genomic Era."

Rockefeller University Trustee Patricia Cloherty, special limited partner of Patricof & Co. Ventures, Inc., spoke on "The Business of Biotech"; Lisa Drakeman, chief executive officer of Genmab A/S, spoke on "Biotech: An Insider's Perspective"; and Teena Lerner, formerly of Pequot Capital



From left to right: Patricia Cloherty, President Arnold J. Levine, Lisa Drakeman and Teena Lerner

Management and a 1983 Rockefeller University graduate, spoke on "Investing in Biotechnology."

The *Women&Science* initiative has grown into one of New York City's most popular philanthropic forums. Last year, the \$300,000 raised through the

Partners in Discovery program supported six women graduate and postdoctoral fellows. This year to date, friends of *Women&Science* have contributed more than \$580,000 toward a goal of \$700,000.



W&S fellows (from left to right) Veronique Haegeli, Jill Donigian, Revati Masilamani and Laura McMullan.



W&S breakfast host Alair Townsend (right) with guest Martina Horner.

2 AROUND CAMPUS

3 IN THE LAB

4 ETCETERA

Take your Child to Work Day

Human Resources will host the annual Take Your Child To Work Day on Thurs., April 26, from 9 a.m. to 3 p.m. Children must be between the ages of 7 and 14 and be accompanied by an adult in order to attend. To register your child, please contact Mary O'Donnell, x8300, or E-mail her at odonnem@rockefeller.edu by Tues., April 17. Registration is limited, so please sign up early.

Flexible Spending Accounts Reimbursement Request Deadline:

Mon., April 16, is the 2000 Flexible Spending Accounts (FSA) reimbursement request deadline for dependent care and health care expenses. Please submit all your 2000 FSA eligible expenses to 21st Century for reimbursement by this date. Any unclaimed balance after this date will be forfeited. FSA Reimbursement Claim forms are located in Human Resources, Founders Hall, Room 103. If you have any questions, please call 21st Century at (800) 686-0685, or Human Resources, x8300.

New library procedure

Effective Mon., April 2, in order to enter and exit the library, patrons must have a current, valid ID card (key card) from The Rockefeller University or an affiliated institution and be registered in the patron database of their institution.



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Brenner to discuss future of computational biology

Sydney Brenner, distinguished professor at The Salk Institute in La Jolla, Calif., will give a special series of lectures entitled "Computational Biology in the Next Decade."

Brenner was born in South Africa and educated at the University of Witwatersrand, Johannesburg (Medicine and Science). He went to Oxford and received a degree of D.Phil., in 1952, working in the Physical Chemistry Laboratory.

After a brief return to South Africa he joined the Medical Research Council (MRC) Unit in the Cavendish Laboratory in Cambridge in 1956, and went on to serve as director of that lab's successor, the MRC Laboratory of Molecular Biology in Cambridge, from 1979 to 1987. In 1987 he became director of the MRC Unit of Molecular Genetics, retiring in 1992 from the MRC. In 1996 Brenner founded the Molecular Sciences

Institute in Berkeley, Calif.

Brenner's early research was in molecular genetics, working with bacteriophages and bacteria; he discovered messenger RNA (with Jacob and Meselson) and, with Francis Crick, showed that the code was composed of triplets. In the 1960s he changed direction and initiated his research on *C. elegans*, establishing it as a powerful experimental system for the analysis of complex biological processes. As a

geneticist, he saw that the techniques of cloning and sequencing would open up new ways of approaching genetics. He turned to studying vertebrate genomics and has established the pufferfish genome as a powerful tool in genome analysis.

The lectures will take place in Caspary Auditorium and are open to the public. Please consult the Calendar for more details.

Fellows "build bridges" between physics and biology

"Biology provides almost an embarrassment of riches for mathematicians at this moment, and the challenge is to identify questions that are interesting both from a biological viewpoint as well as from the viewpoint of quantitative analysis," says Erik van Nimwegen, a mathematical theorist who arrived at Rockefeller in October 2000.

Van Nimwegen is one of three current Fellows in Physics and Biology, and he already is channeling some of his experience using mathematical methods from information theory and statistical mechanics on interdisciplinary problems to some nascent Rockefeller-based collaborations with biologists.

Tsvi Tlusty, another first-year fellow, describes biology as "like another civilization; the whole way of thinking is very different from physics. I study biology the way I would study a foreign language. I need to hear the terms many times, and I don't learn the language just by reading the textbooks; I must talk with people in biology to help me learn what is important."

The Physics and Biology Fellows program, now in its seventh year, is unique among programs for postdoctoral researchers at Rockefeller. Modeled on the Institute for Advanced Study in Princeton, N.J., the program's mission is to accelerate the contributions that physics can make to biomedical science by building bridges between the two scientific communities, which often are separated by barriers of language and technique. The program gives exceptional scientists three-year appointments at an advanced postdoctoral level.

The fellows are independent, so that they may work with any researchers whose interests mesh with their own. Their only requirement is to develop work in the overlap of physics, mathematics or computational science and some area of biology. And by all accounts, the program is successful. All five fellows who completed the program have good academic positions with full license to continue their work in interdisciplinary science.

As John Marko, the first Physics and Biology Fellow at Rocke-

feller in 1994 and now an assistant professor at the University of Illinois at Chicago, says: "While I was at the Rockefeller program, I had the good fortune to spend a lot of time talking with people like David Thaler, Stephen Burley, John Kuriyan, Peter Model and others, who taught me an incredible amount in a short time."

This program's arrangement is a slightly different model of mentoring than that found elsewhere at Rockefeller. While collaborations among laboratories are common, most researchers with Ph.D.s come to the university under the sponsorship of a member of the faculty. At the Center for Studies in Physics and Biology, applications for the Fellows program are "reviewed collectively," says Professor Eric Siggia, "and once they're here we encourage them to attend seminars, meet people in different areas and be independent."

Toyota Professor Mitchell Feigenbaum heads the Fellows program, and fellows often form mentor relationships with more than one of the faculty in



Martin Zapotocky, Erik van Nimwegen and Tsvi Tlusty (left to right) are the current Fellows at the Center for Studies in Physics and Biology.

Physics and Biology, including Feigenbaum, Siggia, Detlev W. Bronk Professor Albert Libchaber and Associate Professor Marcelo Magnasco. Often these mentorships result in collaborative work within the Center.

A weekly seminar in physics and biology provides a special forum for considering the work happening at the cutting edges of physics and biology. Fellows take turns during their time at Rockefeller organizing the series, inviting outside speakers and featuring new work of members of the Center. Several Rockefeller biologists now attend the

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Tomasz lab hosts workshop on bacterial pathogens

As part of an international effort to reduce the global spread of the infectious bacterium *Streptococcus pneumoniae*, the Laboratory of Microbiology, headed by professor Alexander Tomasz, recently hosted a month-long workshop in molecular typing techniques.

The workshop was an integral component of the European Resistance Intervention Study (EURIS), a major, new multinational initiative recently funded by the European Community. EURIS aims to reduce the frequency of carriage of multidrug-resistant strains of *S. pneumoniae* in children attending day-care centers in Sweden, Iceland, France, Portugal and Israel.

"Our goal is to lower the carriage rate of *Streptococcus pneumoniae* in preschool age children in

order to make an impact on the number of cases of related diseases," says Tomasz.

The purpose of the workshop was to standardize the molecular techniques currently being used to analyze bacterial samples in the various EURIS labs. Participants from Ireland, Portugal, Iceland and Sweden arrived at Rockefeller last month and learned molecular typing methods, along with computer-imaging software protocols.

"It's good to come together and learn the same methods," says Gunnell Mollerberg, a participating microbiologist from the Swedish Institute for Infectious Disease Control.

S. pneumoniae, or pneumococcus, represents the most frequent cause of several potentially life-

threatening community-acquired infections, including middle-ear infections, pneumonias, bloodstream infections and meningitis. The annual mortality rate of pneumococcal diseases worldwide is estimated to be several million, roughly the same as tuberculosis. These pathogens tend to live between the nose and throat of healthy people in an area called the nasopharynx. It is from here that they strike out and cause infection.

A particularly dangerous feature of this major respiratory pathogen is the emergence and rapid spread of antibiotic-resistant strains. Previous studies by Tomasz and others have documented the massive geographic spread across national and continental borders of two resistant *S. pneumoniae* strains in particular.

According to Tomasz, nearly half of all disease-causing penicillin-resistant strains of pneumococcus belong to this specific pair of strains. Moreover, these strains have acquired resistance to other important antibiotics as well.

"The secret of the 'success' of these two epidemic clones is one of the most interesting questions we would like to answer," says Tomasz.

The hypothesis that day-care centers might represent a major breeding ground for these pervasive strains first was tested in 1996 by the Lisbon Day Care Initiative, the precursor program to EURIS now headed by EURIS international coordinator Herminia de Lencastre.

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Friday Lectures and Thesis Presentations

THESE EVENTS ARE HELD IN CASPARY AUDITORIUM AT 3:45 P.M. AND PRECEDED BY TEA AT 3:15 P.M. IN ABBY ALDRICH ROCKEFELLER LOUNGE, UNLESS INDICATED OTHERWISE. ALL ARE WELCOME.

FRIDAY, MARCH 23

The Frizzled Family of Wnt Receptors. Jeremy Nathans, Investigator, Howard Hughes Medical Institute, Johns Hopkins University Medical School.

WEDNESDAY, APRIL 4

1:00 P.M. **Thesis Presentation. Multiple Personality Disorder in *Trypanosoma brucei*: Functional Analysis of ESAG8.** Maarten Hoek, Graduate Fellow, RU.

THURSDAY, APRIL 5

Thesis Presentation. Biological Timing: A Developmental Regulator Influences the *Drosophila* Clock. Sebastian Martinek, Graduate Fellow, RU

FRIDAY, APRIL 6

Richard M. Furlaud Lecture. Toward a Chemical Genetics. Stuart Schreiber, Investigator, Howard Hughes Medical Institute, and Morris Loeb Professor, Harvard University.

MONDAY, APRIL 9

Thesis Presentation. Trypanosome Telomeres: In the Loop. Jorge Munoz, Graduate Fellow, RU.

FRIDAY, APRIL 13

Philip Levine Memorial Lecture. Cell Biology of Antigen Presentation. Hidde Ploegh, Harvard Medical School Department of Pathology.

calendar

MARCH TWENTY-THIRD THROUGH APRIL TWENTY-SECOND

FRIDAY, MARCH 23

12:00 P.M. **Mimicking Cellular Proteins or Controlled Cell Damage: Alternative Strategies for the Modulation of Cellular Responses by Bacterial Pathogens.** Jorge Galan, Professor and Chairman, Section of Microbial Pathogenesis, Boyer Center for Molecular Medicine, Yale School of Medicine. Molecular Biology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 11:45 A.M. CONTACT LINDA SMITH, 639-7655. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

MONDAY, MARCH 26

1:30 P.M. **MHC Encoded Class Ib Molecules; Recognition Elements for the Innate and Adaptive Immune Responses.** Mark J. Soloski, Department of Medicine, Division of Molecular and Clinical Rheumatology, The Johns Hopkins University School of Medicine. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

TUESDAY, MARCH 27

10:00 A.M. **TNF Alpha Signaling Activation and Cell Death.** Symposium. Weiss 17th Floor. Contact Jose Perez, 860-441-8806.

4:00 P.M. **Mathematical Slices of Biology.** Misha Gromov, Instituts des Hautes Etudes Scientifiques, Courant Institute. Seminar. B LEVEL CONFERENCE ROOM, SMITH HALL ANNEX. CONTACT ERIK VAN NIMWEGEN, 327-8184.

4:30 P.M. **Beauty Is Skin Deep: Regulation of Epithelial Differentiation in Skin and Hair.** Elaine Fuchs, Amgen Professor, Department of Molecular Genetics and Cell Biology, University of Chicago. MSKCC President's Research Seminar. AUDITORIUM, ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 4:00 P.M.

5:30 P.M. **A Letter to Thoreau.** Edward O. Wilson, Pellegrino University Research Professor and Honorary Curator in Entomology, Museum of Comparative Zoology, Harvard University. Lewis Thomas Prize: Honoring the Scientist as Poet. CASPARY AUDITORIUM.

5:30 P.M. **Structural Studies of a DNA Polymerase Processivity Clamp Loader.** David Jeruzalmi, Research Associate, Kuriyan Lab. Pels Family Center for Biochemistry and Structural Biology Seminar. 110B NURSES RESIDENCE. CONTACT ROSER BUSQUETS, 327-7050. PIZZA AT 5:00 P.M. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

WEDNESDAY, MARCH 28

11:00 A.M. **Chemical Strategies for Smoking out the Endogenous Cannabinoid System and Their Application to Functional Proteomics.** Benjamin F. Cravatt, Assistant Professor, The Skaggs Institute for Chemical Biology and Departments of Cell Biology and Chemistry, The Scripps Research Institute. Seminar. 301 WEISS. CONTACT MICHAEL W. YOUNG, 327-8645.

12:00 P.M. **Adoptive Transfer of EBV-specific CTL's for the Prevention and Treatment of EBV-associated Malignancies.** Cliona Rooney, Associate Professor, Center for Cell and Gene Therapy, Baylor College of Medicine. Seminars in Clinical Research. 110B NURSES RESIDENCE. CONTACT DALE MILLER, 327-8411.

2:00 P.M. **The Story of Heat Shock Proteins and Immunity.** Pramod Srivastava, Professor, Center for the Immunotherapy of Cancer and Infectious Diseases, University of Connecticut School of Medicine. Advanced Topics In Immunology. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

4:30 P.M. **The Cancer Cell Cycle and Drug Discovery.** Nicholas La Thangue, Cathcart Chair of Biochemistry, University of Glasgow, and Chief Scientific Officer, Prolifix Ltd. MSKCC President's Research Seminar. AUDITORIUM, ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 4:00 P.M.

7:30 P.M. **Psoriasis Support Group.** Meeting. 110B NURSES RESIDENCE. CONTACT PATRICIA GILLEAUDEAU, 327-8333.

THURSDAY, MARCH 29

4:00 P.M. **Getting Chromosomes to the Right Place: Meiosis and Male Infertility.** Mary Ann Handel, Professor, Department of Biochemistry and Cellular and Molecular Biology, University of Tennessee, Knoxville. Endocrinology and Reproductive Biology Seminar. 301 WEISS.

4:00 P.M. **Insights into the Genetic and Physiological Basis of Chloroquine. Resistance in *Plasmodium falciparum*.** David Fidock, Assistant Professor, Department of Microbiology and Immunology, Albert Einstein College of Medicine. LFKRI Research Seminar. LOWER LEVEL CONFERENCE ROOM, NEW YORK BLOOD CENTER, 310 EAST 67TH ST. TEA AT 3:45 P.M. CONTACT ROSANNA MARTINEZ, 570-3357.

6:00 P.M. **Bringing the Power of Science to Bear on Drug Abuse and Addiction.** Alan Leshner, Director, National Institute on Drug Abuse, NIH. Centennial Lectures on Science and Society. CASPARY AUDITORIUM. CONTACT BOBBIE LARRAGA, 327-7240.

FRIDAY, MARCH 30

9:00 A.M.-5:00 P.M. **The Biology of Drug Abuse and Addiction: More Tangled than Traffic. Alcoholism: Research Progress and Promise.** Enoch Gordis, Director, National Institute on Alcohol Abuse and Alcoholism, NIH. **The Addicted Brain.** Nora Volkow, Associate Director for Life Sciences. Brookhaven National Laboratory; **Science-based Treatment of Addictive Disorders.** Charles O'Brien, Chief of Psychiatry, Veterans Affairs Medical Center, University of Pennsylvania. **Molecular and Neurobiological Role of Endogenous Opioids in the Addictions.** Mary Jeanne Kreek, Professor, RU. **Molecular Mechanisms of Addiction.** Eric J. Nestler, Professor and Chairman, The University of Texas Southwestern Medical Center, Dallas. **Cloning and Characterization of the Opioid Receptor Family.** Chris Evans, Professor, UCLA. Centennial Symposium. CASPARY AUDITORIUM. ADMISSION IS FREE.

12:00 P.M. **Ras and Rho GTPases and Oncogenesis.** Channing Der, Professor, University of North Carolina, Chapel Hill. Cell Biology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

TUESDAY, APRIL 3

11:00 A.M. **Systems Neurobiology of Genetically Modified Mice: From Plasticity to Pathology.** Joshua Gordon, New York State Psychiatric Institute, Columbia Presbyterian Medical Center. Neuroscience Seminar. 305 WEISS. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

12:00 P.M. **Drowning in a Sea of Data and Starving for Knowledge.** Sydney Brenner, Distinguished Professor, The Salk Institute. Computational Biology in the Next Decade Seminar. CASPARY AUDITORIUM. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

1:00 P.M. **The Masscode Tagging System for High Throughput Single Nucleotide Polymorphism (SNP) Analysis.** Roberto Rodrigues, Director, Business Development, North America, QIAGEN Genomics Inc. Seminar. 305 WEISS. REFRESH

MENTS AT 12:30 P.M. CONTACT TINA BAYER, (800) 426-8157 EXT. 22316. 4:00 P.M. **A Role for Oncogene Activation in the Induction of Genetic Instability in Human Cancer Progression.** Geoffrey M. Wahl, Professor, Gene Expression Laboratory, The Salk Institute. Molecular Pharmacology and Therapeutics Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 3:45 P.M.

WEDNESDAY, APRIL 4

11:00 A.M. **Does *E. coli* Understand Itself?** Sydney Brenner, Distinguished Professor, The Salk Institute. Computational Biology in the Next Decade Seminar. CASPARY AUDITORIUM. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

12:00 P.M. **Mpslp Kinase Family Control of Centrosome Duplication.** Mark Winey, Associate Professor, Department of Molecular, Cellular and Developmental Biology, University of Colorado. Student-Sponsored Seminar. 301 WEISS. PIZZA LUNCHEON AT 1:00 P.M. IN THE WEISS 17TH FLOOR. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

12:00 P.M. **Persistence, Pathogenesis, and Protection in Tuberculosis.** John D. McKinney, Assistant Professor, RU. Seminars in Clinical Research. 110B NURSES RESIDENCE. CONTACT DALE MILLER, 327-8411.

4:30 P.M. **Inheritance of Chromosomes.** Bruce Stillman, Director and Chief Executive Officer, Cold Spring Harbor Laboratory. MSKCC President's Research Seminar. AUDITORIUM, ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 4:00 P.M.

THURSDAY, APRIL 5

10:00 A.M. **Negative Regulation of BMP/Smad Signaling and Ras/MAPK Pathway by an Antiproliferative Protein Tob.** Tadashi Yamamoto, Professor, Department of Oncology, Institute of Medical Science, University of Tokyo. Seminar. 305 WEISS. COFFEE AT 9:45 A.M. CONTACT GENEVIEVE HANNON, 327-8257.

12:00 P.M. **Reconstructing the Past.** Sydney Brenner, Distinguished Professor, The Salk Institute. Computational Biology in the Next Decade Seminar. CASPARY AUDITORIUM. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

CONTINUED ON OTHER SIDE WITH ARTS AND OTHER EVENTS.



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MARCH TWENTY - THIRD THROUGH APRIL TWENTY - SECOND

3:00 P.M. **Brain and Language in Children and Adults.** Elizabeth Bates, Professor, Department of Cognitive Science, University of California, San Diego. Systems Neuroscience Seminar. 305 WEISS. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

4:00 P.M. **Blocks to HIV-1 Replication in Rodent and Primate Cells.** Nathaniel R. Landau, Associate Professor, The Salk Institute. LFKRI Research Seminar. LOWER LEVEL CONFERENCE ROOM, NEW YORK BLOOD CENTER, 310 EAST 67TH ST. TEA AT 3:45 P.M. CONTACT ROSANNA MARTINEZ, 570-3357.

4:00 P.M. **HCV Clearance.** David L. Thomas, Associate Professor, Division of Infectious Disease, Johns Hopkins University School of Medicine. Center for the Study of Hepatitis C Seminar. 301 WEISS. CONTACT PATRICIA HOLST, 327-7047. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

FRIDAY, APRIL 6

12:00 P.M. **Chimeras for Dissecting Complex Phenotypes.** Andras Nagy, Senior Staff Scientist, Samuel Lunenfeld Research Institute, Mount Sinai Hospital. Molecular Biology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 11:45 A.M. CONTACT LINDA SMITH, 639-7655. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

12:00 P.M. **National Library Week Open House.** Christine Fleming, Beilstein; Scott Bard, Institute for Scientific Information; Kevin Monaco, Chemical Abstract Services. Vendor Demonstration. WELCH HALL. REFRESHMENTS AT 12:00 P.M. OPEN TO RU COMMUNITY AND GUESTS.

TUESDAY, APRIL 10

7:00 P.M. **Senses and Sensitivity.** A. James Hudspeth, Professor, RU, and Investigator, Howard Hughes Medical Institute. Genes, DNA and You: The Impact of the Human Genome Project. CASPARY AUDITORIUM. A PUBLIC LECTURE SPONSORED WITH THE 92ND STREET Y. TICKETS ARE AVAILABLE FROM THE 92ND STREET Y AT 996-1100.

WEDNESDAY, APRIL 11

12:00 P.M. **Aging and Cancer: Are Telomeres and Telomerase the Connection?** Jerry Shay, Professor, Department of Cell Biology, University of Texas Southwestern Medical Center. Seminars in Clinical Research. 110B NURSES RESIDENCE. CONTACT DALE MILLER, 327-8411.

4:30 P.M. **Molecular Mechanisms of Lineage Choice and Development.** Stuart H. Orkin, Investigator, Howard Hughes Medical Institute, Professor of Pediatrics, Harvard Medical School, and Chairman, Department of Pediatric Oncology, Dana Farber Cancer Institute. MSKCC President's Research Seminar. AUDITORIUM, ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 4:00 P.M.

THURSDAY, APRIL 12

3:00 P.M. **Studies of Dyslexia.** Guinevere Eden, Assistant Professor, Department of Neuroscience, Georgetown University. Systems Neuroscience Seminar. 305 WEISS. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

4:00 P.M. **Estrogen Regulation of Pituitary Function: A Dynamic Regulatory System.** Margaret Shupnik, Professor of Medicine, Division of Endocrinology, University of Virginia Medical Center, Charlottesville. Endocrinology and Reproductive Biology Seminar. 301 WEISS.

4:00 P.M. **Seeing the CpGs in DNA: Activation of Innate and Acquired Immunity by Pathogen DNA.** Arthur M. Krieg, Professor, Department of Internal Medicine, University of Iowa. LFKRI Research Seminar. LOWER LEVEL CONFERENCE ROOM, NEW YORK BLOOD CENTER, 310 EAST 67TH ST. TEA AT 3:45 P.M. CONTACT ROSANNA MARTINEZ, 570-3357.

FRIDAY, APRIL 13

12:00 P.M. **Cell Division in Fission Yeast—A Model For All Eukaryotes?** Kathleen Gould, Howard Hughes Medical Institute and Department of Cell Biology, Vanderbilt University School of Medicine. Cell Biology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

MONDAY, APRIL 16

1:30 P.M. **Dendritic Cells and the Control of Immunity.** Ralph M. Steinman, Professor, RU. Immunology Seminar. WEILL AUDITORIUM, WMCCU, 1300 YORK AVE.

TUESDAY, APRIL 17

8:00 A.M.—5:00 P.M. **Mind-Body Interactions: An Exploration of the Relationship Between Stress Hormones and Immune Function. Immune Activation of the Stress Axis.** Christine Biron, Brown University. **Immune Activation and Glucocorticoid Receptor Function: Relevance to Immune-based Depression.** Andy Miller, Emory University. **Stress Hormones, Leukocyte**

Trafficking and the Augmentation of Immune Function. Firdaus Dhabhar, The Ohio State University. **Immunological Consequences of Oversecretion of Stress Hormones.** Ron Glaser, The Ohio State University. **Stress, Viral Infection and Wound Healing.** John Sheridan, The Ohio State University. **Immunological Consequences of Undersecretion of Stress Hormones.** Esther Sternberg, National Institute of Mental Health, NIH. **Catecholamine Hormones and Inflammatory Disease.** Cobi Heijn, Universiteit Utrecht. Symposium. WEISS 17TH FLOOR. ADMISSION IS FREE. PRE-REGISTRATION IS REQUIRED BY APRIL 5; ELECTRONIC REGISTRATION IS PREFERRED. TO REGISTER, PLEASE E-MAIL YOUR NAME, INSTITUTION, PHONE AND FAX NUMBERS TO DHABHAR@MAIL.ROCKEFELLER.EDU OR FAX TO (614) 247-6945. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

4:00 P.M. **Mechanisms of Camptothecin Induced Cell Killing.** Mary-Ann Bjornsti, Associate Member, Department of Molecular Pharmacology, St. Jude Children's Research Hospital. Molecular Pharmacology and Therapeutics Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 3:45 P.M.

WEDNESDAY, APRIL 18

12:00 P.M. **Molecular Genetic Analysis of Pneumococcal Virulence.** Andrew Camilli, Assistant Professor, Tufts University School of Medicine. Seminars in Clinical Research. 110B NURSES RESIDENCE. CONTACT DALE MILLER, 327-8411.

4:30 P.M. **Charting Pathways of Tumorigenesis in Mice: Mechanisms and Targeted Therapeutics.** Douglas Hanahan, Professor, Department of Biochemistry and Biophysics, Diabetes and Comprehensive Cancer Centers, University of California, San Francisco. MSKCC President's Research Seminar. AUDITORIUM, ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 4:00 P.M.

THURSDAY, APRIL 19

4:00 P.M. **The Cellular Immune Responses to the Hepatic C Virus and Its Role in Viral Clearance and Disease Pathogenesis.** Barbara Rehermann, Liver Diseases Section, National Institute of Diabetes and Digestive and Kidney Diseases, NIH. Center for the Study of Hepatitis C Seminar Series. 301 WEISS. CONTACT PATRICIA HOLST, 327-7047. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

4:00 P.M. **Therapy for the New Millennium: Using Genetic Medicine to Regenerate Diseased Organs.** Ronald Crystal, Professor of Internal Medicine and Genetic Medicine, WMCCU. LFKRI Research Seminar. LOWER LEVEL CONFERENCE ROOM, NEW YORK BLOOD CENTER, 310 EAST 67TH ST. TEA AT 3:45 P.M. CONTACT ROSANNA MARTINEZ, 570-3357.

8:00 P.M. **Genes, Behavior, and the Sense of Smell.** Cornelia I. Bargmann, Professor and Vice Chairman, Department of Anatomy and Department of Biochemistry and Biophysics, University of California, and Investigator, Howard Hughes Medical Institute. Harvey Society Lecture. CASPARY AUDITORIUM.

FRIDAY, APRIL 20

9:00 A.M. **Minority Career Fair.** Mary O'Donnell, Human Resources Associate, Human Resources. Minority Career Fair. WEISS 17TH FLOOR. CONTACT MARY O'DONNELL, 327-8300.

12:00 P.M. **Genetic Regulation of Mammalian Development.** Richard Behringer, Professor, Department of Molecular Genetics, M.D. Anderson Cancer Center, Houston, Texas. Molecular Biology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 11:45 A.M. CONTACT LINDA SMITH, 639-7655. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

The Arts and Other Events

FRIDAY, MARCH 23

12:00 P.M. **Tri-Institutional Noon Recitals.** Mikhail Yanovitsky, piano. Performing Mozart: *Sonata in a minor, K 310*; Prokofiev: *Sonata No. 7, Op. 83*; Chopin: *Twelve Etudes, Op. 25*. CASPARY AUDITORIUM. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

SUNDAY, APRIL 1

4:00 P.M. **Chamber Orchestra of Science and Medicine.** Spring Concert. CASPARY AUDITORIUM. REFRESHMENTS AT 7:00 P.M. IN THE ABBY LOUNGE.

The science behind the Albany Medical Center Prize: A look at Levine's research on the tumor suppressor p53

The protein the journal *Science* named "molecule of the year" in 1993 and that appeared on the cover of *Newsweek* magazine in 1996—p53—may be the key to unlocking the mystery of cancer. And President Arnold J. Levine's discoveries about the protein and its role in cancer earned him the first Albany Medical Center Prize in Medicine and Biomedical Research. Since 1979, when Levine, then at Princeton University, and David Lane, at the University of Dundee, independently identified the protein, p53 has provided important clues into the tumor process.

Levine told reporters at a news conference last Wed., March 14, that the discovery had its roots in research on a simian virus called SV40, which he began studying in 1968. When injected into hamsters, SV40 causes tumors. A decade later, Levine recalled, Dan Linzer, a graduate student in his Princeton lab, presented him with an X-ray film trace that showed a previously unknown protein. They named this protein p53 (p for protein; 53 for the protein's molecular weight—53,000 daltons).

"I played the skeptic and he played the graduate student, and we had a wonderful drama for a period of three months while he tried to prove to me that this was something new and real," said Levine.

Levine and other scientists originally thought p53 was an oncogene, or a tumor accelerator. In the 1980s, a postdoctoral fellow in Levine's Princeton lab, Moshe Oren, isolated the gene that

we could try to replicate each other's results," said Levine.

Levine said he and Oren found that a single mutation in the p53 protein—a change in the 135th position of the 393 amino acids in the protein chain—allowed tumors to form. They found that p53's normal function is to "act like the spellcheck on your computer," said Levine. "It stops the whole process and says: 'You've made a mistake.'"

The tumor suppressor p53's normal function is "to act like the spellcheck on your computer. It stops the whole process and says: 'You've made a mistake.'"

coded for the p53 protein. Oren later moved to the Weizmann Institute for Science in Israel and found that putting the gene into normal cells made them cancerous. Levine's group, however, found the opposite—inserting the gene into cells prevented tumor formation.

"We sent our gene to Moshe and he sent his gene to us, so

(Bert Vogelstein, working independently at Johns Hopkins University at about the same time, found that p53 was working like a tumor suppressor in humans).

Scientists now know that p53 is part of a complex network with many components. And while the p53 gene is subject to mutation, tumors also can occur in

cells with normal functioning p53. In these cases, other components of the p53 network inactivate or paralyze p53.

In 1992, Levine and his colleagues identified a protein called MDM2 that normally modulates p53. In some cancer cells, too much MDM2 is produced, and p53 becomes bound to MDM2 much like a fist grasped by a hand. Levine's lab now is collaborating with Asso-



After the press conference, Levine returned to his laboratory to explain his research to members of the media.

the development of new drugs," says Levine.

Recently, Levine and colleagues characterized and identified a version of p53 in the fruit fly, an important model organism for the study of a host of human diseases, including cancer. And Levine is a pioneer in the use of DNA microchip arrays, which can analyze the interactions of thousands of genes at one time, to study cancer.

On receiving the award, Levine said, "Everybody in science works very, very hard, and everyone makes important contributions, and you've got to be lucky to make a contribution that also has a medical or clinical impact."

Team identifies an enzyme that regulates action of chronic cocaine

Rockefeller University scientists have found that an enzyme called Cdk5 regulates the action of chronic cocaine in the brain. In a paper published in the March 15 issue of *Nature*, members of Vincent Astor Professor Paul Greengard's Laboratory of Molecular and Cellular Neuroscience and colleagues at other institutions identify Cdk5's role in the long-term changes associated with cocaine addiction. By combining behavioral and biochemical studies, they found that Cdk5 (which stands for cyclin-dependent kinase 5) is a key player in a series of biochemical events that occur in certain brain cells with exposure to chronic cocaine.

Cocaine addiction develops through repeated exposure to the drug. In response, the brain attempts to maintain equilibrium by countering the effects of repeated drug administration. Chronic exposure to cocaine can set a series of chemical reactions in motion, leading to changes in the expression pattern of certain genes that then "feed back" to block the effects of cocaine. This succession of events appears to underlie the adaptive changes occurring in the addictive brain.

"By finding new inhibitors to this pathway, we might find compounds that have a palliative effect, removing the craving for cocaine similar to the way methadone removes the craving for heroin," says Research Associate James Bibb, senior author on the paper.

Cdk5 regulates certain effects of chronic cocaine by controlling the signaling of a neurotransmitter called dopamine.

Dopamine is involved in fine motor control, reward and reproductive behavior, but abnormalities in dopamine signaling are associated with several neurological and psychiatric disorders, including substance abuse. When dopamine is released in the brain, it binds to a receptor and starts a cascade

of biochemical events. Cdk5 is important to this process because it activates a key molecule involved in dopamine signaling called DARPP-32.

"We had shown earlier that DARPP-32 is a major player in the mechanisms by which dopamine produces its effects in the brain," says Greengard, who also is director of the Zachary and Elizabeth Fisher Center for Research on Alzheimer's Dis-

ease at Rockefeller. In the current study, the laboratory was looking for causes and co-factors of addiction.

Cdk5 became an appealing target for this research when co-author Eric Nestler, now at the University of Texas Southwestern Medical Center in Dallas, first found that expression of the Cdk5 gene goes up in mice genetically altered to serve as a model for drug abuse.

In subsequent behavioral studies conducted by Jane Taylor in the Psychiatry Department at Yale University, the effects of the drug roscovitine, which inhibits Cdk5, were assessed in rats that also were exposed repeatedly to cocaine. The results indicated that cocaine-induced increases in Cdk5 levels serve to dampen responses to subsequent drug exposure. The *Nature* paper also shows that repeated exposure to cocaine enhanced the biochemical pathway between Cdk5 and DARPP-32 resulting in reduced sensitivity of the dopamine receptors involved in mediating the behavioral effects of cocaine.



A new finding in the laboratory of Vincent Astor Professor Paul Greengard could have major implications for treatment of addiction.

Other coauthors on the paper include Per Svenningsson, Akinori Nishi, Gretchen Snyder, Zachary Sagawa, and Angus Nairn from The Rockefeller University, Jingshan Chen from the Department of Psychiatry at Yale University, and Charles Ouimet from the Program in Neuroscience at Florida State University.

Funding for the research was provided by National Institute for Drug Abuse and the National Institute for Mental Health.

ETCETERA

Gym relocation

To accommodate the expansion of the Child and Family Center, the campus gym has moved into the Northeast and Southeast Conference Rooms on the 17th floor of Weiss.

Alex Kogan, director of Plant Operations, estimates that the equipment will remain in this interim location through June 11, when structural improvements to the gym's new permanent location (on the sixth floor of Founder's Hall) should be completed.

In the meantime, please note that the gym will be closed on the following dates and times to accommodate events scheduled prior to the announcement that the gym would be moving to Weiss 17:

Tues., March 27, 8 a.m.–6 p.m.

Mon., April 2, 9 a.m.–Wed., April 4, 5 p.m.

Mon., April 16, 4 p.m.–10 p.m.

Tues., April 17, 7 a.m.–6 p.m.

Fri., April 20, 7 a.m.–7 p.m.

Thurs., April 26, 7 a.m.–Tuesday May 8, 5 p.m.

Mon., May 21, 9 a.m.–Thurs. May 24, 5 p.m.

Thurs. and Fri., May 24 and 25, 6 a.m.–12 p.m.

Tree spraying on March 31

The spraying of trees and shrubs throughout the campus grounds will take place on Sat., March 31, starting at 3 a.m. and continuing until 9 a.m. In case of inclement weather, the spraying will take place during the same hours on Sun., April 1. It is recommended that you close your windows, shut off air conditioners, stay out of direct contact with the drift and keep pets inside. If you have any questions, call James Sullivan, x8001.

Tomasz lab continued

The project witnessed the rise of the same two resistant strains of *S. pneumoniae* in preschool age children at day-care centers in Lisbon, Portugal, over a period of several years.

Day-care centers provide an ideal environment for bacteria to thrive in for several reasons. First, preschool age children have immature immune systems, which often fail to mount an attack against foreign pathogens. Hence, the bacteria live undisturbed in the nasopharynx of healthy children. Second, the number of children attending day-care centers is on the rise, placing the children in closer proximity to one another. Add in the behavioral traits of young

children, and day-care centers become massive reservoirs for infectious bacteria.

Finally, the centers also contribute to the rise of multidrug-resistant strains because, according to Tomasz, this age group represents the single biggest market for antibiotics.

EURIS is unique in that it targets not the disease but rather the reservoir of the disease-causing bacteria—the nasopharynx of healthy children attending day-care centers. The various institutions involved in the project will characterize bacterial strains recovered from children in day-care centers using molecular typing techniques, as well as test intervention strategies, including

reduced use of antibiotics, proper dosing regimens, improved hygienic conditions, isolation of carriers and introduction of conjugate vaccines.

Tomasz says that the workshop was a huge success. In addition to learning valuable molecular techniques, the participants and the instructors had a good time.

“We have enjoyed ourselves tremendously,” says Thora R. Gunnarsdottir, a microbiologist from the Landspítallinn University Hospital in Iceland, adding, “The academic culture at Rockefeller is impressive. It's a little academic village in New York City.”

Other participating institutions



Members of the Tomasz lab trained researchers from Ireland, Portugal, Iceland and Sweden in molecular techniques.

include Instituto de Tecnologia Química e Biológica in Portugal; The National Institute of Health and Medical Research (INSERM) in France, Belfast City Hospital in Northern Ireland and Soroka University in Israel.

Nathans continued

During the course of this work, he also discovered a second *frizzled* family member, *frizzled-2* (*Dfz2*). In a collaboration with the laboratory of Roeland Nusse (of HHMI and Stanford University), the Nathans lab showed that the *Dfz2* protein functions as a receptor for *Wingless*, an extracellular signaling molecule involved in patterning in both the embryo and the adult. *Wingless* is a member of a large family of signaling molecules referred to as *Wnt*

ligands. It is now clear that *Wnt* ligands bind to *Frizzled* receptors.

In vertebrates, *Wnt* proteins have been implicated in oncogenic transformation and in embryonic and brain development, processes that are now inferred to be mediated by *Frizzled* receptors by signal transduction pathways that remain to be elucidated in detail. As the biological activities of *Wnt* family members are diverse, it will be of interest to determine the

degree to which differences in *Frizzled* receptors account for the activation of different intracellular signal response pathways.

Nathans is a professor of molecular biology and genetics, of neuroscience, and of ophthalmology at the Johns Hopkins University School of Medicine. As an undergraduate at the Massachusetts Institute of Technology, he studied chemistry and biology. He received a Ph.D. in biochemistry and an M.D. from

Stanford University. Before joining the faculty at Johns Hopkins, Nathans spent a year as a postdoctoral fellow at Genentech. He is a member of the National Academy of Sciences.

Nathans's talk will take place in Caspary Auditorium at 3:45 p.m. and will be preceded by a tea at 3:15 p.m. All are welcome.

Schreiber continued

Chemical Biology and an associate member of the Department of Molecular and Cellular Biology. He also is an affiliate of the Department of Cell Biology at the Harvard Medical School, as well as a member of the graduate programs in biophysics at Harvard University and immunology at the Harvard Medical School. He is the founder and director (with Timothy Mitchison) of the Harvard

Institute of Chemistry and Cell Biology and the scientific director (with Douglas A. Melton) of the Harvard Center for Genomics and Proteomics. He also is a founder and editor of *Chemistry & Biology*.

Schreiber received his B.A. from the University of Virginia in 1977, then carried out graduate studies at Harvard University under the supervision of R.B.

Woodward and Y. Kishi. After completing his doctoral studies, he joined the faculty at Yale University in 1981. He was promoted to associate professor with tenure in 1984 and to professor in 1986. In 1988 he returned to Harvard, where he has remained since.

Schreiber has received several awards for his work and was elected to both the National

Academy of Sciences and the American Academy of Arts and Sciences.

The Richard M. Furlaud Distinguished Lecture is named in honor of the university's chairman of the board emeritus. This year's lecture takes place in Caspary Auditorium at 3:45 p.m. and is preceded by a tea at 3:15 p.m. All are welcome.

Fellows continued

seminars regularly and others are beginning to attend sporadically.

The seminar provides a formal meeting ground for those interested in physics and biology, but there are many informal opportunities for finding common ground, too. Martin Zapotocky, a second-year fellow, met a postdoc from the Mombaerts lab through a mutual friend at the university cafeteria one day. This meeting spurred a series of discussions. Now Zapotocky, trained as a condensed matter

physicist, analyzes genomic data from the lab.

The fellows at the Center for Studies in Physics and Biology make the relationships that they develop with biology-based collaborators look easy. But don't be deceived; it can take quite a while to make the connections that lead to these multifaceted projects. As Zapotocky puts it, “starting an open discussion with somebody about their current work is not always easy. And then when I do meet new people,

they want to know what lab I'm in. I tell them I'm at the Center for Studies in Physics and Biology; most people still don't even know what that is.”

While Zapotocky greatly appreciates the freedom of interaction the Center offers, he adds that one thing is still missing. “We don't yet have biologists contacting us and saying, ‘We thought you might be able to help with this.’ ”

“We may not be able to help with every project, or the people

here may be committed to other projects,” says Zapotocky. “But once there is a widespread understanding that we are here and we want to learn about biological problems and collaborate more with biologists, the Center will definitely live up to its full potential.”

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news & notes

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