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BENCHMARKS

THE COMMUNITY NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

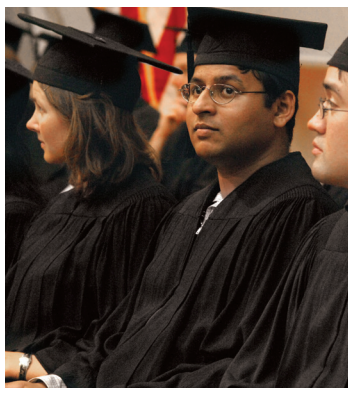
FRIDAY, JUNE 27, 2008

When The Rockefeller University held its first Convocation in 1959, there were only five graduates. As of June 12, nearly 1,000 scientists are recipients of the Rockefeller University doctor of philosophy degree.

This year's festivities began with a graduate luncheon, followed by a cap-and-gown procession across campus to the degree-granting ceremony in Caspary Auditorium, a graduate reception on Peggy Rockefeller Plaza and an alumni reunion reception in Weiss Café.

The class of 2008 is the fourth in the David Rockefeller Graduate Program (named in 2005). It includes 13 men and 13 women from eight countries: Canada, China, England, Germany, India, Japan, Taiwan and the United States. Twenty Rockefeller labs were represented by the graduates and nine of them, members of the Tri-Institutional M.D.-Ph.D. Program, will continue on to medical school. Others will begin careers in academia, industry or other fields.

This annual Convocation issue of BenchMarks *salutes the Rockefeller University class of 2008.*



CONVOCATION 50 YEARS

2008 FOR CONFERRING DEGREES

Thursday, the twelfth of June

For more photos, visit: www.rockefeller.edu/convocation

PHOTOS: BRUCE GILBERT AND ZACH VEILLEUX

Honorary degrees go to three Rockefeller alumni

Fedoroff, Hille and Edelman are honored with the university's highest accolade

by TALLEY HENNING BROWN

Alongside the 26 students who marched in cap and gown to receive their diplomas and graduate hoods on June 12, three Rockefeller alumni returned to the stage where years ago they defended their own dissertations. At this year's Convocation ceremony, honorary doctor of science degrees were presented to plant geneticist and government science adviser Nina V. Fedoroff, class of 1972; ion channel pioneer Bertil Hille, class of 1967; and Nobel laureate Gerald M. Edelman, class of 1960.

Dr. Fedoroff, presented first among the three, is science and technology adviser to United States Secretary of State Condoleezza Rice and to the administrator of the U.S. Agency for International Development. One of the first plant molecular biologists, she studied in the laboratory of Norton Zinder. She worked at the Carnegie Institution of Washington and Johns Hopkins University before joining The Pennsylvania State University, where she is currently on leave from her position as the Willaman Professor of Life Sciences and Evan Pugh Professor, the university's most prestigious professorship. During her early career, Dr. Fedoroff produced one of the first complete gene sequences, pioneered the application of molecular techniques to plants and cloned some of the first plant genes. More recent research has focused on the phenomenon of gene regulation by small RNA molecules, as well as on genes that contribute to plants' ability to protect themselves from environmental stressors.

A member of the National Academy of Sciences and the recipient of a 2006 National Medal of Science, Dr. Fedoroff spoke to the audience in Caspary Auditorium, with a particular message for the women graduates, about the relationship between challenges confronted in the laboratory and those encountered outside it. "I've had the incredible good fortune of participating in the molecular revolutions of the late 20th century," she said. "Ph.D.s, of course, are beginnings, not endings.… Don't shy away from the difficulties; you could have it all."

Bertil Hille is Wayne E. Crill Endowed Professor of Physiology and Biophysics at the University of Washington School of

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BENCHMARKS

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Rudy Bellani receives this year's David Rockefeller Fellowship

by TALLEY HENNING BROWN

PHOTO: ZACH VEILLEUX

When Rudy Bellani filled out only one application for graduate school — to Rockefeller University — his advisers told him he was crazy. "Hundreds of applicants vying for some 20 spots, and me with no backup plan," says Mr. Bellani. "But my advisers were Rockefeller alumni, so they understood my desire to come here." Accepted into the entering class of 2005, he hasn't looked back since. Now a third-year student and a member of Fernando Nottebohm's Laboratory of Animal Behavior, Mr. Bellani is also the recipient of this year's David Rockefeller Fellowship.

Laboratory research was not Mr. Bellani's original career ambition. Born in Bolivia to a family of lawyers and writers, Mr. Bellani grew up in South America and Arizona and originally set his sights on medicine. He attended Arizona State University, where he earned a B.S. in 2005, majoring in psychology and minoring in biology. It was a summer research position in 2004 — intended to bolster his resume for medical school applications — that turned Mr. Bellani irrevocably toward lab science. "What makes a good doctor is the ability to deduce things within already-defined parameters," he says. "What makes a good researcher, as I discovered that summer, is originality."

During a trip to New York City in 2004, one of his advisers at Arizona State, Cheryl Conrad, set up a meeting for him with Bruce McEwen, in whose lab she had once been a postdoc. Dr. McEwen recommended that Mr. Bellani apply to Rockefeller's Summer Undergraduate Research Fellowship program. Mr. Bellani spent that summer in the McEwen lab, studying the development of the stress response in juvenile rats with then-postdoc Russ Romeo. He also did research with Robert Sapolsky, another Rockefeller alumnus, at Stanford University. "He really became the model of the kind of scientist I wanted to be," Mr. Bellani says.

Eager to get a head start on graduate research, Mr. Bellani arrived at Rockefeller in July of 2005, before student housing was available. His 10-week stint living in the McEwen laboratory resulted in the first of many articles he has written for the student-run newsletter *Natural Selections*. Aside from rotations in the labs of Dr. McEwen, Jeffrey Friedman, Nathaniel Heintz and Sidney Strickland, Mr. Bellani took a neuroscience course at the Marine Biological Laboratory in Woods Hole, Massachusetts, and "I fell in love with brain asymmetry," he says. Dr. Nottebohm — who discovered in the 1970s that canaries sing with the left cerebral hemisphere — seemed an obvious match.

Mr. Bellani joined the Nottebohm lab in early 2007 and currently studies the development of brain asymmetry at the molecular and genetic level. "We know that in humans, a great number of brain functions are lateralized — for example, language, moral processing and even face processing," he says. "We don't know why the brain works this way, but it's unbelievably fascinating. The morphology of the brain in disorders like schizophrenia and autism, for example, is always either more lateralized or less lateralized, which makes it all the more compelling." He is also collaborating with Tao Sun, an assistant professor at Weill Cornell Medical College who specializes in asymmetrical brain patterning and neural stem cell development.

Mr. Bellani is hoping to spread some of his enthusiasm to younger students as well. In a two-week course developed with support from the Dean's Office and scheduled for August, Mr. Bellani and other graduate students will teach the basics of neuroscience to 8 to 10 bright — but not necessarily science-oriented — high school students. "Science curriculums aren't usually aimed at getting kids excited, and that leads a lot of students to think they don't like science or, worse, don't have a natural aptitude for it," he says.

Though he knew that Dr. Nottebohm had nominated him for the David Rockefeller Fellowship, Mr. Bellani was surprised when he got a call this spring summoning him to the office of Dean Strickland. "I was mortified. I'd never been called to the principal's office before," he says. "I was so relieved when I found out what it was really about."

"The David Rockefeller Fellowship was established to honor creative scientists who also make significant contributions to the campus in other ways. Rudy's lofty scientific goals and outreach activities make him a perfect fit for this award," says Dr. Strickland.

Mr. Bellani is earmarking the $3,000 prize toward, among other things, his United States citizenship application. "I'm deeply humbled and honored," he says. "And I'm glad that I was so stubborn about wanting to study at Rockefeller."

Honorary degrees (continued from page 1)

Medicine. A student of Clarence Connolly, Dr. Hille is widely regarded as one of the foremost authorities on ion channels, an essential component of the nervous system, as they regulate the flow of ions across cell membranes, serving to control nerve impulses and mediate electrical conduction across synapses. Following degrees from Yale University and Rockefeller, Dr. Hille worked in the laboratories of prominent British physiologists Alan Hodgkin and Richard Keynes before joining the University of Washington, where he has been a professor since 1974.

For his work, Dr. Hille shared the 1999 Albert Lasker Award for Basic Medical Research and the 2001 Gairdner Foundation International Award, with, among others, John D. Rockefeller Jr. Professor Roderick MacKinnon. In his remarks to the graduating students, he exhorted that "the Rockefeller University experiment has succeeded, and in that sense, these honorary degrees are conferred for all the hundreds of graduates [of the university] and for all of our mentors. We three stand for all of them."

Gerald Edelman, a graduate of Henry Kunkel's laboratory and a member of the university's second graduating class, is director of The Neurosciences Institute and president of the institute's publicly supported not-for-profit parent organization, the Neurosciences Research Foundation. He also currently serves as professor and chairman of the department of neurobiology at The Scripps Research Institute.

Dr. Edelman has made significant contributions in the fields of biophysics, protein chemistry, immunology, cell biology and neurobiology, and his early investigations on the structure and diversity of antibodies led to the Nobel Prize in Physiology or Medicine in 1972. Through his research into the regulation of primary cellular processes in the 1970s, he discovered cell adhesion molecules, which guide the development of an animal's shape and form as well as its nervous system. Dr. Edelman is also the author of the theory of neuronal group selection, a Darwinian explanation of brain development based on neural plasticity in response to environment and experience. The author of several books on brain function and human consciousness, he has become in recent years a leading figure in the emerging field of synthetic neural modeling.

Born in New York City, Dr. Edelman earned a B.S. at Ursinus College in 1950 and an M.D. at the University of Pennsylvania in 1954 and came to Rockefeller in 1958. He earned a Ph.D. in two years and then remained as assistant, associate and then Vincent Astor Professor, until leaving Rockefeller in 1992 to head The Neurosciences Institute. During his time here, he also served as assistant and then associate dean of graduate studies. To the class of 2008, Dr. Edelman pressed the importance of one particular component of the scientific endeavor: "Science is imagination in the service of verifiable truth. [It] is in fact a critical component in science, one that will last you your whole life if you're willing to dwell on it and throw away any kinds of judgments that are based on sheer bureaucracy. And in fact, there are some times when imagination leads to a world change."

To read a full transcript of the recipients' remarks, visit www.rockefeller.edu/convocation.

Many happy returns. The Convocation audience applauds for the alumni honorees: top, Nina Fedoroff and Bertil Hille; above, Gerald Edelman, seated between Sidney Strickland and Cori Bargmann.

Gadsby and Muir receive fourth annual teaching awards

by TALLEY HENNING BROWN

The faculty of The Rockefeller University have presided over the hypotheses, experiments and thesis defenses of nearly 1,000 students since the beginning of the graduate program in 1955. Before the Convocation ceremony on June 12, two of these mentors were recognized for their assiduous efforts on behalf of their students. David C. Gadsby, head of the Laboratory of Cardiac and Membrane Physiology, and Tom W. Muir, head of the Selma and Lawrence Ruben Laboratory of Synthetic Protein Chemistry, were presented with this year's Rockefeller University Distinguished Teaching Awards during the Graduate Luncheon.

Established in 2005, the teaching award is given each year to one or two faculty members for contributions that have enriched the university's educational environment. Awardees, who receive a monetary prize and a plaque, are chosen by a committee comprising the university's scientific executive officers.

Dr. Gadsby, who is Patrick A. Gerschel Family Professor, first came to Rockefeller as a visiting student in the laboratory of Paul Cranefield. Upon graduation from University College London, where he received his Ph.D. in physiology in 1978, he was offered an assistant professorship at Rockefeller. He was promoted to associate professor in 1984 and professor in 1991. He is the recipient of an Irma T. Hirschl Career Scientist Award, a K.S. Cole Award from the Biophysical Society and a National Institutes of Health Merit Award, among numerous other honors, and was elected a fellow of the Royal Society in 2005.

Dr. Gadsby studies the mechanisms and signaling pathways that govern the transport of ions into and out of cells, research that carries implications for many essential physiological processes, including secretion of hormones and neurotransmitters, cell fertilization and volume regulation, kidney function and electrical signaling in nerve, heart and muscle cells. In 1986, Dr. Gadsby took over organization of the Neurophysiology course, now called Membrane Biophysics, which he teaches every other year with Professor Sanford M. Simon. "Dr. Gadsby basically puts his life on hold in order to organize and oversee a five-day-a-week class. He attends every lecture and runs every lab," says Rebecca Ahrens, an M.D.-Ph.D. student who took Membrane Biophysics last fall. "And through all of it, he is constantly asking questions and pushing those around him to think about their work in new ways and to try new things."

Dr. Muir, Richard E. Salomon Family Professor, studied at the University of Edinburgh, where he received a Ph.D. in organic chemistry in 1993, and did his postdoc and then served as a senior research associate at The Scripps Research Institute. He began his Rockefeller career as assistant professor in 1996, becoming associate professor in 2000 and professor in 2002. He is also director of the university's Pels Family Center for Biochemistry and Structural Biology.

Dr. Muir's laboratory uses tools of organic chemistry, biochemistry and cell biology to create new technologies for the study of protein function in complex biomedical systems. He began teaching the Chemical Biology course in 1997 and now co-organizes the class with Professor Tarun Kapoor. Chemical Biology is an essential course in the university's interdisciplinary curriculum as it uses the tools of chemistry to explore the complexities of modern biology. Sarah Wacker, a student in Dr. Kapoor's Laboratory of Chemistry and Cell Biology, has taken both Chemical Biology and Biochemical and Biophysical Methods with Dr. Muir. "Both of the courses he teaches are methods-based and during his lectures, I always became excited about trying out each technique on my own. The way Tom teaches simply inspires creativity," she says.

Following tradition, faculty mentors gave congratulatory tributes to this year's graduates. Printed here are the transcripts of those speeches, as they were read on June 12.

Omar Ahmad

D.C.S., Marianopolis College; M.D., C.M., McGill University
Noises off: Two (Pairs of) Views of the Active Hair Bundle
presented by Sidney Strickland (on behalf of A. James Hudspeth and Bruce W. Knight)

All the students at Rockefeller University are exceptional, but some are exceptionally exceptional. Omar Ahmad is one of these.

Omar's family originates from Bangladesh. He arrived at Rockefeller after concluding his undergraduate education and medical degree at McGill University in Montreal. In the course of his medical training, he had conducted some research on waves of excitation in the heart that set him on his subsequent intellectual course.

As you know, the whole idea of science is to get at fundamental similarities between seemingly disparate phenomena. It turns out that there are very general ways of thinking about all sorts of things that exhibit periodic behavior: ice ages, beating hearts, chemical reactions, nerve signals and so on. This mathematical discipline is called dynamical systems analysis. Omar became interested in a newly discovered phenomenon in this sphere, the amplification of sound by the ears.

Most of us think that what an ear does is pretty straightforward: You put sound in a hole on one side, and electrical signals come out a hole on the other side and tell the brain what's been heard. It turns out that much more is going on in there: An ear doesn't just passively receive sound, it actively amplifies its inputs. Our hearing is so sensitive because every faint sound is augmented a hundredfold. In fact, the amplification is so strong that human ears in an ultraquiet environment can actually emit sound: They work so hard that, like a public-address system whose amplification is turned up too far, they actually begin to screech or howl. When the amplifier wears out, which it tends to do with age and as a result of exposure to loud sounds, we become progressively hard of hearing.

In his thesis work, Omar used his experience with so-called dynamical systems analysis by examining a mathematical model for the way in which the ear carries out amplification. In particular, he did a remarkable job of simplifying an extremely complex morass of equations and ferreting out the essential features of the process. His adviser Bruce Knight, a widely experienced mathematical physicist who unfortunately wasn't able to be here today, said that Omar's work was one of the most insightful and sophisticated pieces of mathematics that he had ever seen in a doctoral thesis.

Above and beyond his scientific quality, Omar has been an outstanding contributor to the Rockefeller community. In particular, he has for several years organized the local chapter of Student Pugwash U.S.A., an organization that augments scientific education with lectures on subjects that impact our society, including international health, armaments, the global food supply and so on. This activity is consonant with Omar's acute social consciousness; he is highly aware of contemporary political issues worldwide, and has a strong sense of social justice.

It's also appropriate to say something about dealing with Omar. On the one hand, he is totally frank, utterly without guile, a prince among men. On the other hand, he is gifted with a rare degree of self-assurance that makes even members of our staid faculty want to kill him. Many a person on our campus acts as if he were brighter than everybody else; the syndrome is common enough that it by-and-large goes unremarked. The same attitude in Omar is troublesome only because he is brighter than everybody else. As part of the intimate tutorial process that is part of a Rockefeller education, a succession of faculty advisers have urged him to just shut up. I'm pleased to say that, in the course of time, Omar has picked up on the hint.

All told, Omar is an individual with a rare mathematical talent matched by exceptional dedication to humanity. Where he will go with this combination remains to be seen. He could succeed in conventional research, but might equally find fulfillment in areas of scientific policy or world health. In any event, he is certain to leave a mark through his talent and his altruism.

Kenta Asahina

B.S., The University of Tokyo
Receptors, Neurons and Circuits Supporting Odor Detection
presented by Sidney Strickland (on behalf of Leslie B. Vosshall)

In the summer of 2002, Kenta Asahina left The University of Tokyo and his family behind and moved to New York to pursue Ph.D. training abroad. Although the rest of his class started graduate school in September, Kenta arrived in July so that he could spend a few months acclimating to Rockefeller, New York City, American culture and conversational English. By the end of the summer, he had acclimated perfectly and was in fact completely hooked by American culture, scientific and otherwise.

For his Ph.D. project, Kenta studied how a simple animal — the larva of the *Drosophila* fruit fly — could respond to a large number of different odors.

At the time, there were a few labs using calcium imaging to measure odor responses in adult insects, but no one had attempted this in larvae. Kenta went to an imaging lab in California for a week to learn calcium imaging and returned not only with a viable prep for imaging the larval brain but with data on odor-evoked neural activity in the larval brain. Since then, he has systematically decoded the odor sensitivity of a large number of larval olfactory neurons and tracked that activity to higher areas of the larval brain. These experiments required a dazzling array of novel genetic tools to be built and crossed into flies, something that Kenta did amazingly well. Interestingly, he identified three olfactory neurons that respond to the same fruity odor but that do so at vastly different threshold concentrations. Together with Matthieu Louis, a former postdoc in the lab, Kenta explored how the larval brain processes odor information across a vast range of stimulus concentrations, an important problem for all animals that smell.

In a few weeks, Kenta will leave for a grand European tour, after which he will move to Pasadena to start postdoctoral training at the boundaries of neurobiology and ethology at Caltech with David Anderson, himself a Rockefeller graduate. I expect great things from Kenta and wish him the best in his new life in Southern California.

Helen S. Bateup

B.S., The Pennsylvania State University
The Differential Involvement of Striatonigral and Striatopallidal Neurons in Psychostimulant and Antipsychotic Responses: A Dual Role for DARPP-32
presented by Sidney Strickland (on behalf of Paul Greengard)

Among millions of people who are addicted to different sinful substances, Helen's addiction is truly unique; Helen is addicted to the molecule that is responsible for making us addicted. As a true and fervent addict, she loves and hates her favorite drug with a molecular weight of 32,000. That is why Helen has dedicated many years of her young life to a systematic mutilation of the addictive molecule DARPP-32. She was rewarded. How many drugs can bring a neuroscientist higher than a paper in *Nature Neuroscience*? Maybe *Nature*, maybe *Cell*, but maybe just a sheer excitement that stems from doing something really interesting and novel? I am sure that all of these sweet rewards are ahead for Helen, who remains solidly addicted to science.

She continues to practice science in Bernardo Sabatini's lab at Harvard University, who luckily got HHMI funding to match Helen's spending habits that she developed in Paul's lab. Sabatini will soon realize, however, that Helen, and not HHMI, could be his key to scientific renown. Helen is not only a tireless, courageous and well-spirited investigator, she is also an excellent friend and colleague. We shall miss her in the lab.

Jeffrey A. DeGrasse

B.S., The George Washington University
Proteomic, Bioinformatic and Functional Characterization of the Nuclear Pore Complex of the African Trypanosome
presented by Brian T. Chait

Sometimes one can only wonder at the events that ultimately bring a young person into your lab to do research. Jeff DeGrasse's grandfather, who was from the Cape Verde Islands just off West Africa, was shipwrecked in a whaling bark off Cape Hatteras in the hurricane of 1917 and spent four days adrift in the Atlantic clinging to debris before being saved as one of only two survivors, finally settling in New Bedford, Massachusetts. Jeff's scientific voyage, though hopefully much less traumatic, has nevertheless been a truly great adventure.

Trained in chemistry, he set out to throw light on the evolution of a biological machine that is central to the life of every cell that contains a nucleus. This machine, the nuclear pore complex, directs all molecular traffic that enters and leaves the nucleus. Jeff decided to study the complex in the dreaded sleeping sickness parasite, *Trypanosoma brucei,* an organism that diverged from the branch of the eukaryotic tree of life that gave rise to yeast and man perhaps as far back as two billion years ago. He thought that by comparing the nuclear pore complex from these organisms, he might be able to discern key features that have been maintained over literally billions of years.

This exploration proved challenging in the extreme, requiring a range of strategies that included isolating the components of the machine, identifying them, verifying them as genuine stable components by molecular and cellular biological approaches and ultimately studying them in detail using computational biology. It was impressive to watch Jeff systematically overcome each of the many barriers that stood in his way, all with an extraordinary degree of skill, patience, grace and good humor. His findings, which are many, have profound implications concerning the evolution and function of this centrally important biological machine.

Ilana J. DeLuca

B.S., Yale University
The Hu Syndrome: At the Intersection of Cancer and Autoimmunity
presented by Robert B. Darnell

It is a pleasure to introduce Ilana DeLuca to you. Ilana spent four years working in the laboratory as one of the most focused, albeit relaxed, students I have ever seen. She came to Rockefeller from Yale with an imperfect GPA — hovering somewhere just under an A-plus — after having worked with three powerful scientists: Pietro De Camilli, Steve Burden and Frank Slack. My jaw dropped when I learned about her experiences during her interview for the Rockefeller graduate program, since this was a perfect background to the RNA biochemistry and neurobiology work that we do in the laboratory. I recall well the exciting blackboard talk we had that day, as Ilana immediately stood out as a thoughtful, engaged young scientist with wide-ranging interests. This was reflected in her typically candid application comments: "I can't say exactly what I'd like to study in graduate school. There are so many topics that interest me now — immunology, understanding and treating disease…." In fact, these comments turned out to be prescient.

I was delighted when Ilana signed up to come to Rockefeller and work in our lab, but choosing a project was not so simple. Despite her background in basic science, she became increasingly enamored with human disease. From the beginning, she was a brilliant student. She explored several projects, but in a most outstanding way. For each, she read deeply, thought deeply, worked assiduously, took responsibility, contacting (and impressing) experts in the field about technical issues or ideas.

She finally settled on a clinically related immunology project. This project related to a set of rare diseases our lab studies in which cancer patients develop a clinically important attack against their own tumors that is linked, in ways we don't understand well, to an autoimmune attack against the brain. Ilana set out on an ambitious project to understand how this happens. Working with a postdoctoral fellow in the laboratory, Wendy Roberts, Ilana developed a breakthrough in our ability to see these tumor immune responses directly in our patients. This work trumped the failure of at least three predecessors in the laboratory and led to the discovery of why these prior scientists had failed. There was an unusual — never before seen — type of immune T cell present in these patients, one that we are excited to understand further. At the same time, Ilana modeled how these cells get triggered by looking in mice. This led to a second new discovery: that the immune system looks over — but normally passes up — neurons in the brain, a sort of screening that was not thought to happen. Her science was so good that I found myself surprised, but should not have been, when she walked into my office one day to tell me that she was inspired enough by the ability to study the mechanisms of human disease that she wanted to go to medical school — and off she went. She was so special in the lab that I would have considered insisting that she make sure to return to the lab, but she beat me to it, asking halfway through her first year of medical school if she could spend her first summer back in the lab, where she will come and ponder the ramifications of her thesis work. I'm glad she will be back and look forward to watching her successful career unfold.

Jill Donigian

B.A., Rutgers, The State University of New Jersey
TIN2 Assists TRF2 in Suppressing the ATM-dependent DNA Damage Response at Telomeres
presented by Titia de Lange

When Jill Donigian joined my lab, she already had extensive experience in biomedical research. Jill hails from New Jersey, where she went to college at Rutgers and worked with Nancy Walworth on the DNA damage response in fission yeast. She then did research in the laboratory of Nikola Pavletich at the Sloan-Kettering Institute, where she worked out the structure of SIRT2, one of the histone deacetylases called the sirtuins, which many of you know because of their proposed role in longevity. These enzymes form the basis of the hope that if you drink enough red wine, you may live longer, or if not, at least you had a good time.

Perhaps because her work on sirtuins had peaked Jill's interest in how our cells age, Jill came to my lab to work on telomeres, another biological problem with a proposed link to longevity. As soon as Jill arrived, I realized that she was not only very good in doing experiments but that she is easily the most organized person I had met in my life. Frankly, Jill's highly organized and spotless bench was initially a source of concern to me. I would walk by her bench at the end of the day and see nothing but clean, shiny surfaces and highly organized racks and pipettes. All other benches in my lab are jumbles of gels and tubes and notes scattered and piled up on top of each other. Jill's model bench suggested to me that no experiments were taking place. Nothing is further from the truth. Jill produces data like a machine. But because she is so organized, she can do an impressive number of experiments in a short time yet somehow find the energy to clean everything up and enter her meticulous notes into her lab notebook at the end of the day.

In the years she has been in my lab, she has also managed to gently but persuasively impose order on others, leaving my lab much better organized than it was. Unfortunately, Jill's powers did not extend to her thesis adviser, whose level of organization remains just one step removed from chaos.

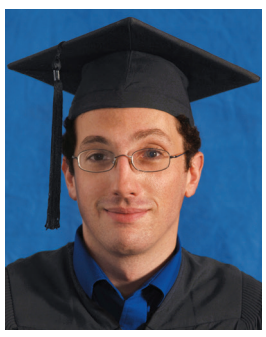
Jill's need to impose order on the world has helped her but has also been a source of aggravation for her. Things inside cells are often messy and usually do not align with the organizational aspirations of a graduate student. When one looks closely into any biological pathway, it is noisy, redundant and often more baroque than one would think necessary. Only when zooming in to the highest level of resolution achieved in crystal structures, or zooming out to the level of an overall pathway read-out, can we get a glimpse of the beautiful design of the inner workings of our cells. In between is the muddy arena of cell biology, and when Jill joined my lab, she had to deal with this morass.

Jill has now cleanly emerged from this mud bath, thesis in hand, publications delivered, more papers to come, important aspects of telomere biology having yielded to her experimental force.

While Jill was working her way through the swamps of cell biology to extract the rocks of hard knowledge from the mud, Jill's extracurricular activities included imposing order on her ever-growing household, which first was expanded with a husband, Dan Salomonsky, and then with a wonderful and wildly popular son, Max Thomas, who will celebrate today with his Ph.D. mom and M.D. dad and tomorrow, on June 13, will celebrate his first birthday.

Yair Dorsett

B.A., The Colorado College
A Role for AID and microRNA-155 in c-myc *to* IgH *DNA Translocations*
presented by Michel C. Nussenzweig



I have had the pleasure of knowing Yair Dorsett for 20 years. I first met him at a dinner party at his parents' home in Boston. At the time, his father, Dale, was a postdoc in Meselson's laboratory and his mother, Ziva, worked with Connie Cepko. Although Yair was only about five years old at the time, it was already clear that this was an exceptional kid and that science was in his genes. So I was delighted three years ago when Yair decided to join my lab after a rotation in Tom Tuschl's laboratory. In Tom's laboratory, Yair learned a great deal about microRNA expression, regulation and metabolism. He came to my laboratory to begin to ask questions about how microRNAs influence the physiology of lymphoid cells. This had not been an area of focus for my laboratory and I therefore assigned him a "safety" project involving chromosome translocations.

Yair is a highly motivated and hard-working student and was able to complete the "safety" project and publish a paper on the etiology of cancer-causing *c-myc/IgH* translocations. In parallel and pretty much on his own, Yair went ahead with his microRNA project. Upon arriving in the laboratory, Yair noticed that the 3' UTR of enzyme that causes translocations, called AID, contains a conserved microRNA binding site. Since AID must be tightly regulated to prevent genomic damage leading to translocations, Yair decided to test whether miR-155 might be responsible for this type of regulation by creating a targeted mutation in the 3' UTR of AID. This was the first such mutational analysis for any microRNA target gene in mammals and showed that miR-155 does indeed regulate AID and that it does so by regulating AID microRNA half-life.

In addition to his work in the laboratory, Yair found time to meet, get engaged to and marry Janjiao Zhou, who is a postdoctoral associate in the Papavasiliou laboratory. As I said, he works fast.

Christopher Gafuik

B.Sc., University of Alberta; M.Sc., McGill University; M.D., University of Alberta
Identification and Characterization of a Viable ras *Hypermorph in* Drosophila
presented by Hermann Steller

The overall goal of Chris Gafuik's thesis project has been to gain insight into the regulation of programmed cell death. All our cells have the ability to self-destruct when they are no longer needed or not useful to the organism, and they do so by activating an intrinsic cell suicide program. Since all the components to carry out death are constitutively expressed in virtually all cells at all times, highly efficient and complex regulatory mechanisms exist to precisely regulate the activity of this death program. The fruit fly, *Drosophila melanogaster*, is a uniquely powerful model system to study how specific cells are selected to undergo programmed cell death in response to different signals. For his thesis project, Chris decided to characterize a *Drosophila* cell death mutant that was previously identified in a large-scale chemical mutagenesis screen. In a textbook example of how to apply a combination of genetics, molecular biology, biochemistry and structural biology insight, Chris defined the molecular nature of this mutant and its precise mechanism of action. First, Chris mapped this allele to the

Drosophila ras gene and demonstrated that it corresponds to a missense mutation that causes a gain-of-function phenotype. Chris provided the ultimate proof for this idea by using x-ray mutagenesis to generate small deletions that revert the gain-of-function phenotype and represent loss-of-function *ras* alleles. Next, based on structural insights, Chris hypothesized that the gain-of-function phenotype of his allele was due to reduced GTPase activity of the mutant protein.

To test this hypothesis, Chris purified both mutant and wild-type proteins and measured GTPase activity. The mutation reduced both the intrinsic and the GAP-stimulated GTPase activity. Finally, Chris used this gain-of-function allele to investigate the in vivo consequences of moderately increased *ras* activity. Chris found interesting phenotypes in several paradigms, including in the proliferation and survival of larval hemocytes, in wing vein formation, in the death of midline glial cells during neural development (increased survival), and in the specification of photoreceptor neurons during eye development (increased numbers of R7 cells).

In all these cases, survival signals coming from the cellular environment have been implicated in regulating cell death, and signaling through *ras* is a major pathway through which these signals are relayed to the cell death machinery. Apart from providing an elegant and convincing mechanistic explanation of why Chris's mutation suppresses apoptosis, his work has given the field the first gain-of-function mutation in the endogenous *Drosophila ras* gene, and this represents a powerful new tool to study the effects of abnormal *ras* activity under physiological conditions.

Chris's project has been technically difficult and challenging in many ways, but Chris was able to overcome many frustrating problems and accomplished a very impressive amount of work. Moreover, he has done all this work with an extraordinary degree of independence. Chris is very bright, dedicated, independent and yet a model lab citizen. He is always open and generous in helping others and has an extremely friendly personality and is completely honest.

Michael E. Hahn

B.S., Brandeis University
Semisynthesis of the Transcription Factor Smad2 Containing Caging Groups and Phosphoaminoacid Analogs
presented by Tom W. Muir

Michael Hahn joined the M.D.-Ph.D. program in the fall of 2000 and after his initial medical training, his interests in protein chemistry led him to join my research group for his Ph.D. studies. Now, Mike had two very clear goals from the outset: firstly, to develop chemical methods to allow the activation of cellular proteins with light; and secondly, to convert my entire research group to Boston Red Sox fans.

Mike became interested in controlling proteins with light since this provides the ultimate spatial and temporal control over biological processes. Many proteins are regulated through posttranslational modification, little chemical tags that are put on and taken off proteins in response to different stimuli and that can tweak what proteins do in a cell. One of the best-known modifications is protein phosphorylation, and because of this, Mike decided that controlling protein phosphorylation with light would be a good place to start his studies. So he started this by figuring out the basic organic chemistry that he needed to do the job. He then moved on by applying this caging chemistry to peptides and then to proteins in a test tube and finally to proteins in a living cell. He was the first to do any of this. By the end of his studies, Mike had become quite the magician and had figured out a way of simultaneously activating both the activity and the fluorescence of a signaling protein called Smad by hitting cells with a single laser pulse. This allowed a detailed analysis of nuclear import of this protein, but the technology should be generally applicable. I'd stress that this is highly sophisticated protein chemistry, and in this regard Mike's work represents the high water mark for my lab so far.

There is no doubt that Mike was terrifically productive in his Ph.D., and you can attribute this largely to his creativity, experimental skills and hard work. But Mike did have a secret weapon, namely his dad, who is here today along with his mother. Parents often get involved in their children's education, usually providing encouragement, support and occasionally by calling up the supervisor for a little chat. But the involvement of Mike's dad was entirely different. On learning about what Mike was up to, namely making proteins, and what the issues were, Mike's dad decided to really help. A plumber by trade, he is at times a scientific instrument maker by inclination. So it was that he came down from Boston and spent several days observing Mike and I in the lab. He then went back to Boston and built in his garage a protein synthesizer. His ingenious design is based on Archimedes's principle of hydrostatics. Incredibly, this machine actually works and really well. Mike's dad has now set a new standard for parental involvement in my lab.

Now, as I mentioned, Mike's second goal was to convert us all to Red Sox fans. In this regard he was persistent and often persuasive and to this day I'm convinced he had a hand in turning my son into a Sox fan. But perhaps his most memorable gambit involved showing us how to sneak into Fenway Park without a ticket. Now as a Yankees fan, personally, this seemed a little bit too expensive to me still, but in hindsight, I now realize that this brazen act was a harbinger of the resourcefulness he was to show time and time again during his Ph.D. studies. Mike has now returned to the wards to finish off his medical training and we certainly wish him all success for the future.

Kristina Marie Hoke

B.S., The College of William and Mary
A Novel Phosphorylation Site in the Telomeric Protein TRF2 Is Regulated by the ATR Kinase and Plays a Role in Relieving Replication Stress at the Telomere
presented by Titia de Lange

Kristina Hoke is a biomedical fellow in our terrific Tri-Institutional M.D.-Ph.D. Program. Kristina and I met during the Frontiers course, a course for the M.D.-Ph.D. students in the first two years of their training. Already at that early stage, Kristina pointed out an inconsistency in my reasoning and this was the beginning of a great series of contributions Kristina made to the lab's research progress. In addition to her own scientific discoveries, Kristina has been the lab's editor for many years. She has carefully read and critiqued every single paper I wrote in the past five years. Unlike mine, Kristina's prose is crisp, clean and uncluttered. Such lucid writing reflects a logical mind with strong analytical skills, which will serve her throughout life, no matter what aspect of the biomedical sciences she will choose in the end. Kristina's imprint is noticeable in every one of the papers we published in the last few years and I can only hope that at this juncture, which marks the completion of my opportunity to train Kristina, conversely, she is now done training me.

Despite spending long hours in the lab on her experiments, Kristina has built up a vibrant life in New York City: Her Facebook page, an interesting source of information, lists 177 friends. More importantly, Kristina became a public figure in politics when she decided to take charge of the ailing organization of Manhattan Young Democrats, completely revitalizing and revamping its operation and working hard for local and national elections. She has now passed on her leadership position of what is now an extremely active and rejuvenated organization, so that she can fulfill her obligations in the clinic. She exemplifies one of the great and inspiring new movements in politics — young, highly motivated and involved voters. I wish her colleagues great success in fall.

As a leader in the NYC democratic community, Kristina gets blogged and I just want to quote one blog on her because, while it is not my style of commentary, I agree with what it says.

Here is the quote from the blog on a meeting of the Manhattan Young Democrats: "Kristina Hoke was looking good, looking in control. I admire her strength. You should go to one of her meetings. The entire hierarchy knows who calls the shots. She is sharp too. When I went online on her, some of the things that showed up were journal-style biological sciences articles. Maybe she is one of those rocket scientists."

Well, Kristina is not a rocket scientist, but she is, in every way, a Rockefeller scientist and one we can be proud of.

Yun-Yuan Hsu

B.S., The University of Texas, Austin
Structural Analysis of Cif, a Cyclomodulin from Pathogenic Escherichia coli
presented by C. Erec Stebbins

As anyone who stares at a medium-rare hamburger with trepidation knows, infections with pathogenic *Escherichia coli* are a serious matter. Worldwide, infectious diarrheal disease is second only to cardiovascular disease as a cause of death. But most *E. coli* bacteria that we encounter are not pathogenic and in fact are necessary citizens of our gastrointestinal tract, contributing to our metabolism, for example, by producing vitamin K. So what makes a normally commensal organism pathogenic? Almost always it is the acquisition of virulence genes that are added to the bacterial chromosome.

When she joined my lab, Yun decided to work on one such virulence protein of *E. coli*. Called Cif, for cycle inhibiting factor, the protein induces an arrest in the cell division cycle. Such an activity prevents cells of the immune system from proliferating, as well as preventing the turnover of infected cells in the intestine. For her thesis work, Yun was able to produce the Cif protein in large amounts, purify it and grow crystals of the molecule. She then used the technique of protein x-ray crystallography to record the scattering of x-rays from the crystal, using this diffraction pattern to reconstruct the chemical model of the protein. This model revealed that Cif is a divergent member of a broad family of enzymes found in both normal and pathogenic contexts. Yun showed that the key active-site amino acids revealed by the crystal structure were critical for cell cycle arrest in an infection model. She then showed biochemically that the protein possessed the predicted enzymatic function. Finally, she was able to identify a host protein that interacts with Cif and show that this interaction is critical for the cell cycle arrest phenotype. This host protein in fact turned out to be a regulator of cell cycle progression.

Yun's thesis is therefore a very rich one, with work in biophysics, protein biochemistry, structural biology and infection biology. In all these things, Yun was always an avid learner, a highly mature and professional scientist and a positive and friendly force for the laboratory. I know that everyone in the lab will miss her as she heads out to California for her postdoctoral training and, of course, we all wish her the greatest success.

Heather Anne King

B.S., The College of William and Mary
Structural and Biochemical Analysis of the Drosophila *Protein Period, a Conserved and Essential Component of the Circadian Clock*
presented by Michael W. Young

Heather came to my group with an unusual background in chemistry. Rockefeller has a collaborative program with Cornell University that seeks to identify exceptional students in chemistry. These students train for a first year in Cornell's large chemistry department and can then choose to perform a rotation in a lab at Cornell, Rockefeller or another affiliate institution. Some of these students develop a significant interest in biological problems.

Heather chose to work with us on a problem related to circadian clocks. These control our cycles of sleep and wakefulness and many other biological rhythms.

Although she came to my lab with little experience in biology and could easily have picked up just enough to carry out her project, Heather became deeply interested in all areas of our lab's work. Heather decided to work on a project involving protein crystallography, not at all an area covered by our group before. Heather would have to solve technical problems, as they arose, without substantial day-to-day input from other members of my laboratory. She instead arranged to be coadvised by Brian Crane at Cornell University and assembled a working collaboration with

a crystallographer, André Hoelz, who is affiliated with Günter Blobel's lab here at Rockefeller. She arranged all of this on her own, and her plan worked remarkably well over the course of her graduate studies.

Heather is a very effective experimentalist. Her project focused on a key portion of the Period protein (PER) that is essential for circadian rhythms in animals ranging from fruit flies to humans. Heather solved this structure and showed in extraordinary detail how pairs of PER proteins may physically combine with each other to affect circadian behavior.

Heather's successes in the laboratory have run parallel to her successes at home. Two sons were born to Heather and her husband while she was a student here. Heather and her family will now move on to a new series of postdoctoral adventures at the National Institute of Environmental Health Sciences in North Carolina.

William J. Lane

B.E., Hofstra University
The Molecular Evolution of Multisubunit RNA Polymerases
presented by Tom W. Muir (on behalf of Seth A. Darst)

Bill Lane has a very rare combination of talents — he is a card-carrying wet-lab biochemist and x-ray crystallographer. In addition, Bill is an exceptionally gifted computer scientist/bioinformatition. During his initial years in the lab, Bill undertook a structural analysis of how bacterial RNA polymerase controls "alternative" gene expression. This involves the expression of genes that are not normally required for survival of the cell under default conditions but are required under specialized circumstances, an example being expression of genes that are essential for bacterial pathogens to survive in the host organism during an infection. Bill's laboratory work and deep analysis of his structural results led to insights that apply to a large fraction of all alternative bacterial gene expression and led to an important paper that was published in *PLoS Biology*.

Around this time, Bill and I had become aware of the fascinating work of Rama Ranganathan at the University of Texas Southwestern Medical Center. Rama has been developing sophisticated sequence analysis methods that are being used to uncover relationships within protein sequences that are not self-evident from static views of a crystal structure. This, combined with experimental validation by mutagenesis, was uncovering unexpected allosteric networks within small protein domains. What could such an analysis reveal about the structure and function of a large macromolecular machine like the RNA polymerase, an assembly comprising dozens of such domains?

Bill took it on without hesitation, despite my warnings that it might not even be possible, or that the results might be so complicated that we may never understand them. Bill completed a series of analyses that are so rich in insights that we are still grappling with the reparation of a number of manuscripts that will be born from this work. I firmly believe this work will ultimately be recognized as classic in understanding the structure-function relationship of RNA polymerase specifically and in a macromolecular machine in general.

Bill is now greatly missed in the lab, mostly for raising the intellectual bar of scientific discussions, for his countless contributions to keeping all of our computers running smoothly and for his high-volume contributions to political discussions (with the volume being a strong function of the number of beers). I myself miss Bill greatly; I'm extremely grateful and consider myself very lucky that he joined my group and I wish him the best in his medical studies.

Ariel Levine

B.S., Brandeis University
The Role of GDF-3 in Patterning the Early Embryo
presented by Ali H. Brivanlou

Since Ariel Levine first joined my laboratory as a graduate student in 2002, I have come to cherish her, both as a person and as a scientist.

Her acute intuition has allowed her to unravel embryological problems at the molecular level, achieving excellence concomitantly in embryology, molecular biology and biochemistry. She is not afraid of complexity or the overwhelming amount of work required to demonstrate a point unequivocally. I can attest without hesitation that Ariel is the best, most talented graduate student with whom I have had the pleasure to work. Ariel is an extraordinary young scientist. She has the qualities that distinguish those few researchers who have the ability to make a lasting impact on their field. Neuroscience has been recently characterized as "a discipline of promise not yet of accomplishment." I agree and suggest that scientists such as Ariel are the kind who can bridge that gap.

You are the only faithful student I have.
Although you will leave eventually,

Remember that I have not been making
myself shallow,
with making you eminent.

Just remember, when you teach,
you don't have to fear
that you'll be drained.

The command comes to speak,
and you feel the ocean
moving through you.
Then comes, Be silent,
as when the rain stops,
and the trees in the orchard
begin to draw moisture
up their stems.

Randy Lindquist

B.A., Williams College
Immunological Voyeurism: Visualizing Dendritic Cells with Transgenic Mice
presented by Michel C. Nussenzweig

Randall Lindquist is a native of New York City and a graduate of Stuyvesant High School and Williams College. He was inspired to go into medicine and science by his brother's struggle with and cure from promyelocytic leukemia. It was therefore natural for Randy to join a laboratory that works on leukocytes and lymphoid malignancies when he came to the Rockefeller-Cornell-Sloan Kettering Tri-Institutional M.D.-Ph.D. Program.

When Randy came to the laboratory he decided that he wanted to try to directly visualize dendritic cells in living tissues to learn about how they interacted with other cells, and in particular T cells, to initiate immune responses. To do this, he used a new technology called two-photon laser scanning microscopy, which allows you to make movies of cells in living mice. To see the cells, he collaborated with Hedda Wardemann to create mice in which dendritic cells glowed fluorescent green. What he saw in the microscope when he looked in living tissues is that dendritic cells exist in dense networks that look like vast colonies of sea anemones with long and constantly moving colorful extensions. He found that T cells are constantly moving through these networks in search of antigen and when they find a dendritic process with the cognate antigen, they stop to receive their marching orders and only leave after a prolonged contact-dependent conversation. Randy then collaborated with Tanja Schwickert, another Ph.D. student in the laboratory, to examine the dynamics of B cell responses in germinal centers. Randy's work led to two first-author publications in *Nature Immunology* and a collaborative paper in *Nature*. Randy is now finishing medical school at Cornell before his next adventure in science and medicine.

Veena Mandava

B.A., Williams College
Identification and Characterization of Histone Modifications in Trypanosoma brucei
presented by George A.M. Cross

Veena came to us from Williams College with the highest honors and the Leverett Mears Prize in Chemistry. Among other achievements, she was a writing tutor at Williams, and her excellent writing skills were greatly appreciated, by me, when she wrote her thesis.

Veena was my first M.D.-Ph.D. student — a generally brilliant but sometimes highly strung breed — and joined my lab somewhat by default, having started what she thought would be her thesis project at one of the sister institutions apparently without checking the tenure prospects of her adviser there.

With me being ancient, there was no concern on that score.

Veena undertook a somewhat chemical project whose results provided the foundation for exciting ongoing work in the lab. Veena's early months in the lab were punctuated by research reports for which she also provided home-cooked lunches. This tradition later lapsed, perhaps once she felt experimenting on us was no longer necessary as clinical opportunities came closer.

Veena gave me one memorable piece of advice about the clinical world: If you want to know how surgeons compare, ask an anesthesiologist. It is probably too soon to say if Veena will follow in the footsteps of her anesthesiologist father. All she has to do for now is to focus on her final clinical year.

Revati Masilamani

B.Tech., Anna University
Understanding Dendritic Cell Regulation of Peripheral Tolerance in Polyclonal T Cell Repertoires
presented by Michel C. Nussenzweig

Revati was born and educated in India, where she received her bachelor's degree from the Anna University in Madras. She came to Rockefeller with an interest in immunology and infectious diseases and joined my laboratory to work on dendritic cell biology, focusing on trying to understand the role of these cells in maintaining immune tolerance in the steady state.

Revati initially worked with another graduate student, Daniel Hawiger, on developing a method for specifically targeting antigens to dendritic cells in situ in order to understand the function of these cells in the organism.

Together they developed a way of engineering monoclonal antibodies to dendritic cells so they could carry specific antigens to these cells in vivo. Her work showed that antigen delivery to dendritic cells in the steady state leads to profound T cell tolerance by a variety of different mechanisms. However, all of the initial work on dendritic cell-induced tolerance in vivo done by Revati was performed using transgenic T cells, since these cells are easy to track and characterize. As a critical follow-up to try to further understand the tolerance problem, Revati has characterized the tolerance response in intact mice with a diverse T cell repertoire. These experiments have important potential implications for the development of antigen-specific immune therapies in a variety of conditions like allergy, arthritis and lupus that involve excess immune activation.

In addition to her work in the laboratory, Revati has also found time to take advantage of New York and her passion for dance. She has won prizes as a performer of the Indian classical dance form called Bharatanatyam. Revati will take some well-deserved time at home to visit with her parents before pursuing postdoctoral research in microbiology.

Hilleary B. Osheroff

B.A., Reed College
Dividing the Preplate: Characterization of the Earliest Neuronal Populations of the Cerebral Cortex
presented by Mary E. Hatten

Hilleary's doctoral thesis concerns early phases of cortical development. In her research, Hilleary has harnessed the tools of molecular biology, mouse genetics and live cell imaging to study cells thought to provide the scaffolding for the assembly of neuronal layers in the brain. Understanding the rudimentary steps required to build the cortex is expected to provide insights into what goes wrong in developmental diseases such as autism, epilepsy or mental retardation.

As a student in my lab, Hilleary has held the highest standards. Her faculty advisory committee had to try and convince her that her experiments were not boring, rather to be written up as her thesis. In addition to her talents at the bench, Hilleary is a wonderful writer; her thesis was accepted without revision — that is the first time I have heard of that happening, let alone experienced it with one of my students. In addition to her research in my lab, Hilleary has taken the initiative to volunteer as an after-school tutor and teacher outside of her thesis research project. For the last three years, she has devoted several hours a week to working with children from New York City public schools. She is keenly interested in developing new ways to bridge science and secondary education.

Ulf Peters

Vordiplom, Humboldt University; M.S., The University of Tennessee, Knoxville
Small Molecules as Probes for Cell Division and Intracellular Transport
presented by Tarun Kapoor

When Ulf joined my lab he told me that he wanted to figure out exactly how a drug works, one of the most challenging problems at the interface of chemistry and biomedical research. I soon learned that Ulf is fearless, hardworking and brilliant. He is also one of the most strong-willed individuals I know. He decides what to do and when to do it. Not much can change his mind. If it is December and a sunny day, and Ulf decides it should be warm, he wears shorts and sandals, ignoring wind chill, heckles or advice.

In the course of his graduate work, Ulf developed a strategy to discover new drug-like chemicals. Using this approach, he identified a chemical that inhibits a protein whose function goes awry in cancer cells. He examined, at the limit of what can be resolved by a light microscope, precisely what happens in a single cancer cell treated with this drug-like chemical. His work provided insight into how certain molecularly targeted therapeutics, currently in clinical trials, may induce cancer cells to die. At several steps during this work, Ulf's iron will overcame disappointments, driving him to make new and important discoveries. Ulf has been an extraordinary graduate student who has become a great friend of mine. I am going to miss him.

Edmund Ching Schwartz

B.S., University of Virginia
Controlling Bacterial Transcription: Regulation of the Sigma Factor
presented by Tom W. Muir

Ed Schwartz joined my group in the fall of 2001 following undergraduate studies at the University of Virginia. It soon became clear to me that Ed was an unusual talent. I can vividly recall the day he excitedly described to my group a new chemical technology he had conceived that would allow rapid activation of cytokine receptors in cells using small molecules. This would be a breakthrough, he predicted. I agreed; what's more, I gave him my personal guarantee that his idea would work. This conviction was well founded, you see, since a very well-known Harvard chemist had spent over a decade using Ed's technology in a series of quite famous and, of course, published experiments. Nonetheless, I was deeply impressed that Ed had thought this up independently, and so after I'd given him a quick tour of the university library, I unabashedly used every trick in the book to recruit him into my lab.

Now a few months later, Ed burst into my office with another one of his ideas. This time he wanted to chemically synthesize proteins inside a living animal, and by co-opting a process called protein splicing and by doing so, gain control over their function. Now I was pretty sure that no one had done this before, and to be honest, I thought he'd been spending a little too much time in the subterranean depths of the library. But Ed was adamant that he wanted to do this, and so because chemistry professors are famously averse to any creature with more than two legs, Ed forged a very fruitful collaboration with Mike Young's lab to turn fruit flies into protein synthesis factories. Ed had to solve many protein engineering problems in trying to reduce his idea to practice, but with the kinks eventually worked out, he then showed that indeed his approach could be used to turn on the activity of an enzyme in a living fly in a rapid and tunable manner. Using his methods, one can simply feed a fly a drug and within minutes generate a protein from premade pieces, in other words, performing protein chemistry inside a living animal. This opens up many new experimental possibilities.

I didn't think any of this was possible, and I think this serves as a beautiful illustration of the late Arthur C. Clarke's first law, which, when translated from the original English, states "When a senior professor" — that would be me — "states that something is possible, he's almost certainly right. When he states that something is impossible, he's very probably wrong." I would also note that in addition to the work in flies, Ed carried out a tour-de-force biochemical structural analysis of a bacterial sigma factor, which ultimately unearthed the mechanism by which a protein is autoregulated. In other words, Ed did enough work for two Ph.D.s.

Ed has now moved on to bigger and better things, as a postdoc in Richard Axel's lab at Columbia, and being such an exceptional scientist, I know he'll do well over there. However, we do miss him and his sometimes arcane sense of humor around the lab. Among other things, Ed has an ability to conduct an entire conversation using nothing but quotes from *The Simpsons*. This could be disconcerting, as when he quoted to me Homer Simpson as saying, "Facts are meaningless. You could use facts to prove anything that's even remotely true."

Amandeep Singh

A.B., Cornell University
Cellular and Molecular Mechanisms Underlying Leptin's Metabolic Effects
presented by Jeffrey M. Friedman

In 1900, Theodore Roosevelt published an article that put forth his view of all American men, writing, "He must not be a coward or a weakling, a bully, a shirk or a prig. He must work hard and play hard. He must be clean minded and clean lived, and able to hold his own under all circumstances and against all comers." It is surprisingly difficult to find a definition of an all-American and I quote this description because it captures, far better than I could, precisely how I think of Amandeep Singh.

Amandeep was born in India and moved to the U.S. at the age of five. He grew up in Buffalo and attended college in Ithaca, working hard and excelling in all manner of things. As an undergraduate at Cornell, he was a National Scholar, Presidential Research Scholar and vice president of the student body. He also established the Cornell Bhangra team. Bhangra is a traditional Punjabi dance and is extremely strenuous. Amandeep both participated in and choreographed Bhangra dance routines and has appeared at the Hollywood Music Awards and on MTV and the BBC. The Bhangra team that he established was recently voted "Number-one Best All Time" by *Punjab Online*. Amandeep graduated from Cornell University summa cum laude and entered the Tri-Institutional M.D.-Ph.D. program.

With support in the form of a Paul and Daisy Soros Fellowship for New Americans, considered to be equivalent in prestige to a Rhodes Scholarship, Amandeep joined my laboratory and with characteristic insight, vigor and fearlessness set out to dissect the molecular mechanisms by which the hormone leptin regulates energy expenditure.

In 1760, the physician Malcolm Flemyng wrote, "Not that all corpulent persons are great eaters, or all thin persons are spare eaters. We daily see instances to the contrary." This is because body weight is controlled not just by how much we eat but also by how many calories we burn. The hormone leptin acts to regulate body weight both by reducing food intake and by also increasing energy expenditure. How leptin increases energy expenditure has been a great mystery and Amandeep set out to see if it did so by regulating the function of mitochondria. Mitochondria are a cellular organelle that can be most simply viewed as the cellular furnace, the place where nutrients are burned to generate energy. What Amandeep found was surprising; despite increasing systemic energy expenditure, leptin reduces mitochondrial function in the liver, the tissue that we thought was likely to be a key target of leptin's metabolic effects. Instead of burning calories in response to leptin, the liver exports nutrients to other tissues where they are burned. This sets the stage for future studies aimed at defining the peripheral tissue that burns energy in response to leptin. It has long been known that increasing caloric expenditure can reduce weight, the main problem being that the compound best able to do this, dinitrophenol, carries with it the minor toxicity of sudden death. In the long term, Amandeep's work may provide a foundation for safely increasing energy expenditure.

Amandeep now returns to Weill Cornell Medical College to complete his medical training. He plans to pursue a career as a physician-scientist with a clinical and research interest in cardiology. It has been a great pleasure to work with Amandeep. His scientific abilities and personal presence have enriched my laboratory, though his growing prowess in poker is beginning to impoverish me.

In closing, I would like to quote Ian O'Connor writing about the New York Yankee Hideki Matsui in *USA Today*: "Sometimes it only takes a trip to India by way of Buffalo to find a real all-American."

Sriram

B.Tech., Indian Institute of Technology Kanpur
High-precision Measurement of Bacterial Growth Rates: A Step toward Understanding of Deleterious Fitness Effects of High Mutation Rates
presented by Stanislas Leibler

Sriram, also known as Sri Ram, came to New York from Kanpur, India, where he did his undergraduate studies at the Indian Institute of Technology. His fields of study there were computer science and technology. Not surprisingly, therefore, Sriram feels at ease with computers and computations, but you would be mistaken if you classified Sriram as just your regular computer wiz.

Sriram's interests and skills are broad. They range from computational biology to experimental microbiology, by way of electronics and optics. During his stay in our laboratory, Sriram participated in several projects. Some of them had a playful quality to them, such as the building of a microfluidic sorter for tiny translucent worms. Others were less playful, like the study of cooperation in synthetic communities of yeast. The main topic of his thesis, however, was a serious piece of engineering.

Motivated by the problem of understanding mutator strains in bacteria, Sriram built a novel apparatus to precisely measure the growth rate of bacteria over long periods of time. He can now follow bacterial growth over weeks by measuring their generation times every hour with a precision of tens of seconds. To give you an idea of this performance, let me transpose it onto the human time frame: This would roughly correspond to measuring the average lifespan of all human beings every year, over 2,000 years, with a precision of one month. Of course, feeding and babysitting bacteria is much, much easier — although Sriram still spent many days doing this in a 100-degree environmental room.

Sriram has other passions apart from science: In particular, he loves trains. Maybe when riding them in his beautiful native India he learned the lesson that he implemented so well in his experimental set-up: Speed and "high throughput" may be important, but precision and reliability are even more crucial.

Pete Stavropoulos

B.S., State University of New York, Stony Brook
Crystal Structure and Mechanism of Human Lysine-specific Demethylase-1
presented by Günter Blobel

Pete had already a great deal of exposure to research when he joined Rockefeller's graduate program. His first experience in a laboratory was during his freshman year of undergraduate studies at Stony Brook. From that point on he became fascinated by research. He spent time in several laboratories, including that of Nouria Hernandez at Cold Spring Harbor Laboratory, Serge Fuchs at Mount Sinai School of Medicine and Michel Nussenzweig here at Rockefeller. With each of these mentors, he coauthored papers. After joining my laboratory, I persuaded Pete to expand his research interests from biochemistry and molecular biology to structural biology.

He began his studies with a subcomplex of the nuclear pore. This work greatly contributed to the elucidation of the atomic structure of the subcomplex, and it was recently published in a seminal paper in *Cell*. Parallel to this project, he began to work on a chromatin-modifying enzyme, the histone demethylase LSD1, and solved its atomic structure. This work was published and was one of the top 10 most downloaded papers in 2007 in all of the *Nature* journals. Recently, Pete has solved the atomic structures of two more key proteins associated with chromatin and is now preparing this work for publication. Altogether, these are spectacular and extraordinary accomplishments. Key in this astounding productivity has been the collaboration and mentorship of André Hoelz, a postdoc in our laboratory who received his training from former Rockefeller University professor John Kuriyan.

Besides being so productive and creative at work, Pete is also an exemplary family man. He and his wife Vasiliki have a beautiful little boy named Angelo. Although born in America, Pete maintains close ties to his Greek heritage. Both his mother and father were born in Greece but are now residing in the United States. Pete loves his ancestral homes, which are located in Sparta and in a small village in Laconia. In addition, Vasiliki is from the Greek island of Chios. They now have three places to choose from when visiting Greece. Pete will stay on in our laboratory to complete his work.

Megan Elizabeth van Overbeek

B.A., University of California, Santa Cruz; D.E.A., Université Pierre et Marie Curie
The Apollo Nuclease Binds to TRF2 and Protects Telomeres in S Phase
presented by Titia de Lange

The third student to graduate from my lab this year and the speaker at today's luncheon, Megan van Overbeek, joined my lab with a keen interest in chromosome biology and a deep affection for microscopy. Megan's last name is of Dutch origin, leading me to continually make the mistake of pronouncing it the Dutch way, including today. However, when I first met Megan, I did not think she was Dutch, or American: I was convinced she was French. It took me a while before I believed that despite her fluent French, her ability to make exquisite mousse au chocolat, her flair and her undergraduate studies on kinetochores at the Institut Curie in Paris, she is in fact not French at all. Megan is from that other country where the food is better, good wines are local and people know how to enjoy life: California.

Megan began her studies on the protection of mammalian chromosome ends by focusing on Rap1, an ancient protein at telomeres, part of the shelterin complex that is central to our work. But among the shelterin components, Rap1 had been largely ignored by us, not getting the attention it deserved. Arguably fitting with Megan's general approach to life, which is marked by originality, she was attracted to the Rap1 project, which placed her outside the mainstream.

Another one of Megan's personality traits led to her discovery of the new shelterin-associated protein she wrote her thesis on. Megan had done extensive mass spectroscopy analysis of the Rap1 complex in collaboration with Brian Chait's lab. Nothing new came out of that. Most students would have given up at this point, accepting the results of the world's leading mass spec lab as the ultimate truth. Not Megan. Because authority means little to Megan, she insisted that there were proteins in the Rap1 complex that her studies with the Chait lab had missed. So she pressed on and eventually got what she wanted, not untypical of Megan.

As a result, two years ago, Megan gave birth to a new member of the growing family of nucleases in the shelterin complex and affectionately named her nuclease Apollo in reference to its similarity to another nuclease called Artemis. At about the same time, Megan gave birth to her daughter Helena, in Greek mythology a half sister of Apollo, sharing Zeus as a father. But in Megan's saga, Apollo and Helena share a mother.

Despite the arrival of Helena, Megan did not neglect Apollo, making a series of discoveries on its function that formed the center of her thesis. She now has returned to her first love in my lab, Rap1, trying to get to the bottom of its function before she moves on to postdoctoral research. Megan brings to science a powerful combination of originality, independence, determination and genuine excitement that will form a fertile ground for future scientific discovery.

Lisa C. Zaba

B.S., Stanford University
Dendritic Cells in Normal and Inflamed Human Skin
James G. Krueger

Lisa Zaba came to the laboratory almost at the end of medical school (at Weill Cornell Medical College) for what I thought was only a short research elective. Instead, the research she began intrigued her so much that she elected to join the M.D.-Ph.D. program and to obtain a Ph.D. degree in addition. As such, Lisa joins a long tradition at Rockefeller of physicians who have elected to obtain graduate degrees in research after completing medical training. Lisa's work has been focused largely on dendritic cells in the skin, cells that are immune sentinels in the skin and that probably orchestrate cutaneous immunity to pathogens and other environmental agents.

Lisa's work has been absolutely critical in defining how to identify these cells in the skin, and she has discovered critical properties of these cells in both healthy and in diseased skin, in which psoriasis has largely been used as a model of autoimmunity. Based on Lisa's work, the work of many scientists will carry forward to discover how these cells function in protecting the skin against pathogens, how these cells will participate in other autoimmune diseases and how these cells may fight against cancer. Wisely, Lisa has chosen to continue her training in medicine and to specialize in diseases of the skin, in which the cells that she discovered are likely to play critical roles in orchestrating diseases of this important human organ. Lisa has been a leader as a biomedical fellow with publication of a significant array of important papers and I expect her to be a leader in academic dermatology in the future. Lisa, best of luck to you, although you do not need my blessing of luck for future success.

Julie Biyuan Zang

B.A., University of California, Berkeley
Identification of Loss of Specific FMRP-RNA Interactions as a Cause of Fragile X Syndrome
presented by Robert B. Darnell

It is a pleasure to introduce Julie Zang to you, on behalf of myself and her thesis coadviser, Jennifer Darnell. After working with us for five years, I would characterize Julie as a brave pioneer, both in her choices in the laboratory and her choices in life. Julie comes from a family of doctors; when she graduates from the M.D.-Ph.D. program here, she will be the fourth generation in a row to receive an M.D. degree, which must make her family extremely proud. Julie had a special challenge in this charge, as she immigrated to the U.S. from Shanghai at age 17!

After coming here, she began college studies at a junior college in California as a math whiz, competing on national teams, and was so outstanding that she transferred to UC Berkeley, where she continued as a straight-A student (with a few exceptions, but those were A-plusses). While there, she volunteered to work in the lab of Ray Stevens on the crystal structure of botulinum toxin. This succeeded in crystallizing her interest in science, but to quote from her Rockefeller application, she found she was "fascinated by the human body — the product of billions of years of evolution."

This might seem a bit of an overstatement, since we normally think of mammals as having evolved over only the past 200 million years, but in fact, this comment actually turned out to be prescient with respect to her thesis. Julie had become especially interested in human neurological disease, which led her to our laboratory five years ago. There, she set out on a very challenging, cutting-edge and bold project — a brave pioneer. She set out, and succeeded remarkably, in developing a new animal model for human mental retardation. This model was remarkable in that only a single point mutation in one protein leads people to be impaired in their thinking. Mutations in this gene, encoding the fragile X mental retardation protein, are responsible for the commonest cause of human mental retardation. Unfortunately, for years after the gene was cloned, only a small inkling has been developed regarding how the encoded protein works. Julie's new mouse has led to a very important conclusion, which is that defective regulation of RNA by the fragile X mental retardation protein is likely the primary defect in the disorder. And going back to evolution, it is now thought that such RNA regulation is not only important in human cognition but was elemental in the very earliest development of life — billions of years ago — from the so-called RNA World Hypothesis.

The ambitious nature of Julie's project is that she did not stop her work with the development and understanding of this new mouse, although that was certainly a thesis's worth of work in itself. Instead, she pushed herself to go on and ask what RNA the fragile X mental retardation protein might be regulating. She has helped pioneer a new means of approaching this question and brought us a long way toward finally developing true insights into what underlies this important human neurologic disease. She is a rising star, and we wish her well as she moves through her medical studies toward a return to the world of translational research.

The next generation

Many of this year's graduates are moving on to new pursuits outside of Rockefeller University, but this fall, 29 new scientist-scholars will fill the ranks. The university's screening committee — overseen by the Dean's Office and including Sean Brady, Hironori Funabiki, Charles Gilbert, Magda Konarska, James Krueger, Stanislas Leibler, Marcelo Magnasco, F. Nina Papavasiliou, C. Erec Stebbins and Leslie Vosshall — vetted applications from 558 prospective students over the winter months and pared them down to 84.

Next year's new students include 13 women and 16 men, from 14 countries: Argentina, China, Germany, India, Japan, Korea, Kuwait, Russia, Singapore, Taiwan, Tanzania, the United Arab Emirates, the United Kingdom and the United States. Their alma maters include: Aga Khan University Medical College, Auburn University, Brown University, Columbia University, Ewha Womans University, Fordham University, Harvard University, Haverford College, National Taiwan University, National University of Singapore, New York University, Princeton University, Scripps College, Stanford University, The University of Tokyo, the University of Auckland, the University of Auckland Medical School, the University of Buenos Aires, the University of California, Berkeley, the University of California, Davis, the University of Cambridge, the University of Kansas, the University of Konstanz, the University of Madras, the University of Pennsylvania, the University of Wisconsin, Madison, Western Washington University and Yale University.