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SCIENCE FOR THE BENEFIT OF HUMANITY

BENCHMARKS

THE COMMUNITY NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

FRIDAY, JULY 8, 2011

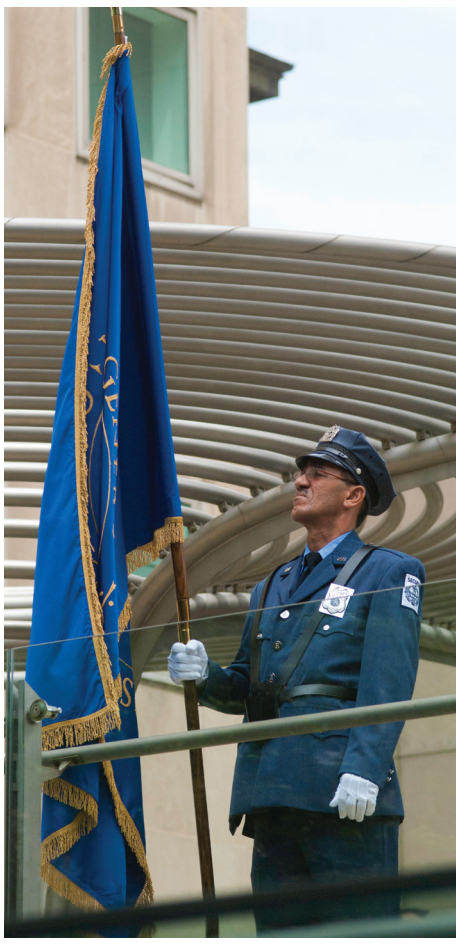
This year's Convocation celebration honored 23 graduates, bringing the total number of Rockefeller alumni to 1,070. Events included an evening reception for the graduates and their families, a luncheon, the traditional cap-and-gown procession across campus, a formal ceremony in Caspary Auditorium and a campus-wide celebration on the Peggy Rockefeller Plaza.

Members of the class of 2011 — 11 men and 12 women — come from seven countries: Brazil, England, Germany, Greece, India, Italy and the United States.

Of the 18 students in the Ph.D. program, 16 will go on to postdocs, one will be working in biotech and one is undecided. The five participants in the Tri-Institutional M.D.-Ph.D. program will return to medical school to finish their medical degrees.

This annual Convocation issue of BenchMarks *salutes the 2011 graduates of the David Rockefeller Graduate Program.*

To view more photos visit www.rockefeller.edu/convocation.



CONVOCATION 2011

FOR CONFERRING DEGREES

Thursday, the sixteenth of June

BENCHMARKS

Marc Tessier-Lavigne, President
Jane Rendall, Corporate Secretary
Joe Bonner, Director of Communications

Zach Veilleux, Executive Editor

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PHOTOS: HEATHER LASZLO AND ZACH VEILLEUX

Honorary degree recipients unraveled secrets of scent

Linda B. Buck, a member of the Fred Hutchinson Cancer Research Center in Seattle, and Richard Axel, University Professor at Columbia University, who have together unraveled the mechanisms that underlie our sense of smell, are this year's recipients of honorary doctor of science degrees.

Drs. Buck and Axel shared the 2004 Nobel Prize in Physiology or Medicine for their discovery of odorant receptors and their work to understand the organization of the olfactory system.

Dr. Buck received bachelor's degrees in psychology and microbiology from the University of Washington in 1975 and her doctoral degree in immunology from the University of Texas Southwestern Medical Center at Dallas in 1980. She joined Dr. Axel's Columbia laboratory as a postdoc in 1982, and began studies related to how odor molecules in the environment are detected by specialized receptors in the nose and then translated by the brain into specific smells.

She moved to the department of neurobiology at Harvard Medical School in 1991, and joined Fred Hutchinson in 2002. She has been a Howard Hughes Medical Institute investigator since 1994, and has received numerous awards.

"There's a critical link between basic science and medicine and therefore society," Dr. Buck said in accepting her degree. "Basic science gives us the knowledge of the mechanisms that underlie biological systems — how they function. It is that knowledge that allows us to understand what goes wrong in disease, and with that understanding finally to be able to develop preventions and cures for diseases."

PHOTOS: ZACH VEILLEUX

Honoris causa. Linda B. Buck, top; Richard Axel, bottom.

Dr. Axel's work has integrated molecular biology with problems in neuroscience, with the expectation that genetics could interface with neuroscience to approach the tenuous relationship between genes, behavior and perception. His studies, with Dr. Buck, on the logic of the sense of smell revealed over a thousand genes involved in the recognition of odors and provided insight into how genes shape our perception of the sensory environment.

Dr. Axel received his bachelor's degree from Columbia University in 1967 and his medical degree from Johns Hopkins School of Medicine in 1970. He returned to Columbia for residency and two fellowships, then moved to the National Institutes of Health as a research fellow. He joined the faculty of Columbia in 1974 and has been an investigator at the Howard Hughes Medical Institute since 1983. He has also been the recipient of numerous awards.

"Our society depends upon its universities to defend the freedom of inquiry, to answer bad ideas with better ideas. Indeed, freedom of inquiry is a condition for the very existence of a university, and it is fragile," Dr. Axel said in accepting his degree. "What drives us in the work of science is precisely the sense that there are truths out there to be discovered, that once discovered will form a permanent part of human knowledge. The acquisition of knowledge is an end unto itself … science endeavors to understand, not to control."

Joseph Luna named David Rockefeller Fellow

BY ZACH VEILLEUX

Joseph Luna, a native of El Paso, Texas and a graduate of Yale University who is exploring host-virus interactions at the RNA level, has been awarded this year's David Rockefeller Fellowship. The David Rockefeller Fellowship has been presented annually since 1998 to an outstanding third-year student who demonstrates exceptional promise as both a scientist and a leader.

After receiving his bachelor's degree in molecular biophysics and biochemistry in 2006, Mr. Luna remained at Yale for two additional years, further honing his laboratory skills as a National Institutes of Health Post-baccalaureate Research Scholar and as a research assistant. He enrolled at Rockefeller in 2008, and almost immediately formulated an ambitious project to study the involvement of RNA in host-virus interactions using next-generation sequencing developed by Robert B. Darnell. The idea required setting up shop in both the Laboratory of Neuro-oncology, which Dr. Darnell heads, and in the Laboratory of Virology and Infectious Disease, led by Charles M. Rice.

"Joe was someone who could lead such a joint project with enthusiasm and scientific vigor," says Dr. Darnell. "Joe is simply having a blast, as fully engaged as one could possibly hope for from a young scientist."

The technique Mr. Luna is using, called HITS-CLIP, gives researchers a global view of the RNA sequences linked to a particular protein. Although Dr. Darnell's lab has been using it to understand the role of small RNAs in neurons, it had not previously been applied to questions of viral infection and replication. Using the hepatitis C virus — and occasionally other viruses — Mr. Luna is working to understand what's going on at the RNA level that permits certain viral invaders to ultimately take over a susceptible host cell.

"At the cellular level, the battle between a virus and a host cell is typically waged by proteins," says Mr. Luna.

PHOTO: ZACH VEILLEUX

Fellowship festivities. Marc Tessier-Lavigne presents the David Rockefeller Fellowship to Joseph Luna at the Convocation luncheon.

"What I'm trying to do is observe an analogous struggle at the informational, that is, the RNA level. The CLIP technique is allowing me to measure the changes that occur in the RNA that give either the virus or the cell an advantage."

Drawn to microbiology for its relatively clear and well-defined problems — and to Rockefeller for its unstructured approach to learning as well as its storied past in virology — Mr. Luna has made the most of his time here, becoming involved not only with two distinct labs, but with several extracurriculars as well. He is an avid historian, who spends his spare moments looking into the past to create a map of legendary spaces on the university's campus. He writes regularly for the student publication *Natural Selections*, and has served on its editorial board since his first year at Rockefeller. He is a serious runner, and completed last year's New York City marathon in about three and a half hours. And, using a small letter-press that he keeps in his apartment, he also practices the art of old-fashioned type-setting.

"Joe's dedication to science, his outstanding research accomplishments and his community service exemplify what Rockefeller seeks to cultivate in its graduate students," said Marc Tessier-Lavigne, the university's president, during his presentation of the fellowship. "These characteristics — independence, commitment to science, leadership and community spirit — are the qualities that Joe has so clearly demonstrated."

Teaching awards honor Hang and Kapoor

Howard C. Hang, head of the Laboratory of Chemical Biology, and Tarun Kapoor, head of the Laboratory of Chemical Biology and Microbial Pathogenesis, were the recipients of this year's Rockefeller University Distinguished Teaching Awards. Established in 2005 to recognize outstanding individual contributions to the university's educational environment, the teaching awards are presented each year to one or two faculty members. Chosen by a committee that includes the university's scientific executive officers, awardees receive a plaque and a monetary gift. Dr. Kapoor (right, with President Marc Tessier-Lavigne) began teaching chemical biology with Tom Muir in the winter of 2002 and the two faculty members repeated the course in the fall of 2004, the spring of 2007 and the spring of 2009. Dr. Hang co-organized, with Nina Papavasiliou, an immunobiology course which the two faculty members taught together in 2009; Daniel Mucida will join them in 2012. Dr. Hang is also joining Dr. Kapoor for the 2012 chemical biology course, which is a required class for all students in the Tri-Institutional Chemical Biology Program. The teaching awards are presented by the president each year during the Convocation luncheon.

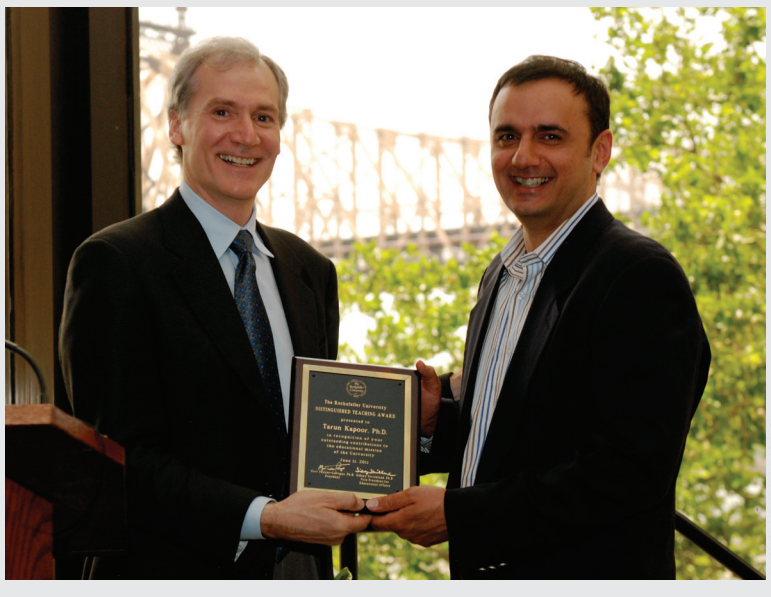
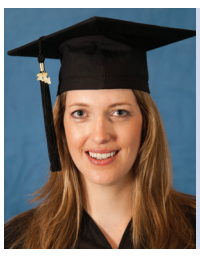


PHOTO: HEATHER LASZLO

The 2011 Graduates

Following tradition, faculty mentors gave congratulatory tributes to this year's graduates. These are the transcripts of those speeches, as they were read on June 16. Students in the Tri-Institutional M.D.-Ph.D. Program are marked with an asterisk.



Erika deWyllie Billick*

presented by Sarah Schlesinger on behalf of James G. Krueger

B.S., University of California, Los Angeles
Defining the Genomics of Normal Human Epidermal Keratinocytes and Melanocytes

Erika Billik came to the Tri-Institutional M.D.-Ph.D. program by way of California. She did her undergraduate work at UCLA. It was in California at boarding school that she came to discover the microscope as a window into the wonder of the natural world. As a 16 year old high school student she found her life's work in her AP biology class, when she was introduced to microscopy.

At Rockefeller Erika has extended the use of the microscope to complete her thesis work in Jim Krueger's lab. Her work has been rooted in careful microscopic observations and characterized by the same sense of wonder about what she has observed as was her work in high school. Erika has coupled careful light microscopic observation (18th and 19th century technology), with laser capture technologies and gene array analysis (truly cutting-edge 21st century technology) to define at the most refined level what distinguishes malignant melanoma, the most lethal tumor of the skin, from its normal precursors. This is significant work from a conceptual point of view. However, as Erika is a budding physician-scientist, it also has protein translational importance. This work sets the stage for Erika and her colleagues to discover at the level of individual gene expression what distinguishes normal skin and a common mole from potentially lethal malignant melanoma, and potentially to exploit these differences to discover targets to combat this tumor.

In addition to her scientific work, while here at Rockefeller, Erika has been an active member of the community, contributing her warmth and expertise for the benefit of others. She co-chairs the AIDS teaching program at Cornell Medical school, is an active board member of Project Lipstick and has mentored younger female M.D.-Ph.D. candidates through FACES.

After finishing her thesis work Erika has returned to her clerkships at Cornell. Next year when she graduates from medical school she intends to pursue an academic career in dermatologic and molecular pathology.

Anne Helen Bothmer

presented by Michel C. Nussenzweig

B.S., Worcester Polytechnic Institute
The Role of 53BP1 in DNA Double-strand Break Repair

Anne Bothmer is originally from Germany; her parents are both in the sciences, her mother a chemist and her father an engineer. Anne came to the U.S. for college, where she starting out thinking that she might be an engineer but ended up with a degree in physics. Along the way she caught the biology bug and decided that she wanted to stay here to go to graduate school in a place that would allow her to explore her new passion.

She ultimately chose to work on DNA repair and cancer, focusing on molecular mechanisms that repair DNA lesions. She discovered how DNA ends are normally protected from nucleases during repair and how this contributes to the selection of the DNA repair pathway that ultimately fixes the broken ends. Her work is published in *Cell*, *Molecular Cell* and the *Journal of Experimental Medicine*.

When you first meet Anne she seems quiet but she is an incredibly strong individual and brilliant student who does exceptionally well when she is challenged. But she is not all work and no fun — in her spare time Anne is an accomplished sailor and a glider pilot.

After graduating, Anne will be going to Harvard Medical School for a postdoctoral fellowship in cancer biology in the laboratory of Paolo Pandolfi.

Michael Chiorazzi*

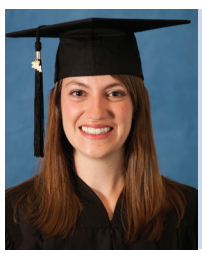
presented by Shai Shaham

B.A., Williams College
DRE-1, a Conserved F-box Protein, Regulates Apoptosis in Caenorhabditis elegans

It's a pleasure for me to be here today for Mike's graduation. Mike is an M.D.-Ph.D. student. As many of you probably know, students accepted to these double degree programs are selected in part on the basis of being able to navigate multiple realms simultaneously. Mike was very good at this. For example, he independently applied for a fellowship from NIH to support his studies, a project no one in my lab has undertaken, and received it. These fellowships are quite competitive, and being granted one suggests not only a superb academic record, but also the ability to write well. This latter quality is one that I have admired in Mike from the outset of his studies.

In my lab, Mike studied the process of programmed cell death: the normal death of cells during animal development. Carine Maurer, a former M.D.-Ph.D. student in the lab, discovered that one of the cells that normally dies during development of the nematode *C. elegans*, the organism which we study in the lab, does so in a slightly strange way. For this cell, programmed death did not require some of the components required for the deaths of other cells. Carine identified a number of mutant *C. elegans* strains that blocked this unique cell death, and Mike joined the lab to figure out what was wrong in these animals. He worked diligently to understand one of these mutant strains, but the experiments were complex and the results inconclusive. Turning to another strain, he hit pay dirt. He identified a new gene regulating cell death. Furthermore, this gene was highly conserved in other organisms, including humans. Mike worked out the genetic details of how this gene functions, and established a collaboration with his former mentor at NIH to examine whether the gene may be disrupted in a certain subclass of cancers. It was.

Mike's interests in both medicine and basic research found an exciting partnership in his project. One might call it serendipity; alternatively, as Louis Pasteur once remarked: "Chance favors the prepared mind." Mike is now back at medical school. I look forward to following his interweaving of science and medicine as his career develops.



Nicole Creanza

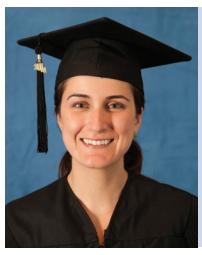
presented by Fernando Nottebohm

A.B., Harvard College
Assessing the Phylogenetic and Cultural Content of Learned Song

We know what birds are on campus by their song: there is a cardinal, a mockingbird, a couple of robins and several house finches and house sparrows. But what determines the properties of their song that make them so easy to recognize?

Nicole Creanza came to The Rockefeller University from Harvard, where she had become interested in evolutionary biology and linguistics. While here, she wondered whether the similarities and differences between the songs of different species reflected their genetic distance. Joel Cohen and Shai Shaham helped her design programs for sound analysis that quantified degrees of genetic and acoustic separation. Nicole found that those two were strongly correlated. This came as a surprise because the birds she compared learn their song by imitation. Now we know that though imitation confers freedom to produce a diversity of sounds, it is still ruled by genetic restrictions that set limits to a bird's tune, a beautiful example of the interplay between rules and freedom.

On top of her scientific prowess Nicole was also my lab's chef. She saw to it that during our periodic laboratory meetings, there was always a delicacy for the palate, which she invented and cooked. Nicole has already transferred to Stanford, where she continues to study the evolution of sounds used in communication.



Shelli F. Farhadian*

presented by Leslie B. Vosshall

S.B., Massachusetts Institute of Technology
Regulation of Feeding Behavior in Anopheles gambiae *and* Drosophila melanogaster

I am pleased and proud to introduce Shelli Farhadian to you today. Shelli is the daughter of a high-achieving Persian family that left Tehran after the fall of the Shah to pursue new opportunities in America. Prior to enrolling in the Tri-Institutional M.D.-Ph.D. program, Shelli earned a B.S. in mathematics from the Massachusetts Institute of Technology in 2003, and was awarded a Fulbright Scholarship to India where she recruited families into a genetic study for risk factors for early-onset heart disease. This experience kindled Shelli's interest in pursuing research on infectious disease.

In my laboratory, Shelli played the enormously important role of initiating a new mosquito research program. She was the first in my group to work on the malaria mosquito and because we were not set up to breed these animals, she spent several weeks at the Centers for Disease Control in Atlanta dismembering, and being bitten by, mosquitoes. She went on to investigate how the mosquito transcriptome responds to blood feeding, and to do parallel work in *Drosophila* to ask how these flies respond behaviorally to periods of fasting and how fasting affects the fly transcriptome.

For her achievements, Shelli was awarded a Paul and Daisy Soros Fellowship for New Americans and a highly competitive NIH predoctoral fellowship. In my lab, Shelli will be remembered for her buoyant and friendly personality. Over the years she became my friend and confidante in the lab and in the various exotic locales to which we traveled with the Gates Foundation, including an unforgettable trip to Beltsville, Maryland with today's honoree, Richard Axel.

Shelli has returned to the clinic and appears to be greatly enjoying her time as a physician-in-training. She will be a great and compassionate clinician and we will miss her.

Robert Jonathan Fenster*

presented by Cori Bargmann on behalf of Paul Greengard

A.B., Harvard College
B.A., University of Cambridge
Cell-type Specific Translational Profiling in Huntington's Disease Mouse Models

Robbie Fenster is a renaissance man: he not only excels as a student, writer, wine taster, marathon runner and Boggle player, but also as a molecular neuroscientist and doctor-in-training.

Robbie graduated from Harvard University *summa cum laude* in 2003, and went on to receive a B.A. in English Literature from Cambridge University. Before he joined Paul Greengard's lab, Robbie already had strong ties to Rockefeller, working here first as a high school student in Bruce McEwen's lab, and then returning as an undergraduate SURF student and research assistant in Leslie Vosshall's lab. Upon beginning medical school at Cornell, Robbie was drawn to Rockefeller yet again, this time to Paul's lab for a one-year HHMI-funded research fellowship. The fellowship research was so successful that Robbie decided to switch into the Tri-Institutional M.D.-Ph.D. program in order to complete a Ph.D. in Paul's lab.

Robbie's doctoral thesis is truly fitting for a physician-scientist — he has used a model organism to study the molecular mechanisms underlying the devastating pathology of Huntington's disease. His studies have revealed previously unappreciated changes in the cells most affected in the disease, work that may lead to the identification of novel therapeutic targets. In particular, his work may reveal why it is that the huntingtin protein is so toxic to medium spiny neurons, even though it is expressed widely throughout

the nervous system and body. Demonstrating his dedication to bringing together clinical experience and basic biology, Robbie has also spent time in a clinic interacting with patients suffering from Huntington's disease. Robbie, congratulations on your Ph.D., and we wish you the best for your future scientific endeavors.

Zak Frentz

presented by Shai Shaham on behalf of Stanislas Leibler

B.S., Stanford University
Long-term Quantitative Microscopy: From Microbial Population Dynamics to Growth of Plant Roots

In biology, building simple scientific instruments is considered old-fashioned nowadays. Custom-made microscopes, for instance, are exhibited in glass cabinets as museum items, mainly to demonstrate how glorious (or tedious) past research was. After all, why should one build a microscope today if research can be made so much more productive thanks to fully automatic, top-of-the-line, user-friendly Leicas or Nikons?

Nonetheless, during his Ph.D. years, Zak Frentz built 10 holographic microscopes, at the risk of appearing old-fashioned and unproductive. For his study of repeatability in ecology, Zak had to simultaneously follow population dynamics in several copies of a model microbial system. Microscopes thus had to not only be precise and reliable, but also compact and cheap. Zak and his friend Seppe Kuehn managed to achieve these goals by altering popular SLR cameras and simple laser diodes. They are now collecting an amazing amount of unique data.

As if this were not enough, Zak decided to build yet another machine. His scanning light-sheet microscope allows him to follow the growth and regeneration of *Arabidopsis* roots. Like its 10 holographic brothers this 11th instrument gathers very-long time series of three-dimensional images.

But "going up to 11" and "sustaining it for long," like the *Spinal Tap* guitars and amplifiers, is not Zak's main achievement. During his Ph.D., he moved beyond mathematics and theoretical chemistry, which he studied at Stanford, and has become a true polyglot, at ease with the language of biology and physics. In addition, he taught his adviser not only about *Spinal Tap* but also about many subtle points of optics and microbiology. Watching him progress in science, the answer to the famous question: "Where can you go from there?" is obvious: Zak will go off the scale!

Felice Kelly

presented by Paul Nurse

B.S., Bradley University
Spatial Control of Cdc42 Activation Regulates Cell Width and Growth Zone Formation

Felice is fast. In fact she is very fast, having been placed 22nd in the women's 2009 New York City marathon. She also enjoys cycling, rock climbing, kayaking, going to the Met Opera, playing Scrabble and most charmingly of all, knitting. But what she likes best is thinking about research and doing experiments in the lab.

She came to my lab to work on how cells determine their shape. All living things have characteristic shapes and that also applies to cells, but how they achieve this is not well understood. Felice used a fission yeast strain collection which had every gene independently deleted, and by visual inspection she identified those gene functions which when absent made the yeast cells wider. She then used these mutants to investigate how a fission yeast cell determines its width, and found that it is controlled by a gradient of activated Cdc42 located at the growing end of the cell. Her explanation was quite simple: if the gradient extends further, then the growth area is greater and the cell is wider. She found out that the genes she had discovered controlled the extent of this gradient and so the width and shape of the cell.

Felice also likes to organize. At the annual winter lab retreat, she organized a night time snow Olympics, with tug-of-war, snow soccer, hula hooping and kickball all in the dark and all in 12 inches of snow. And she is interested in helping the community, most notably as a long time member of the university's green task force.

She moves from Rockefeller to Stanford to take up a postdoc working on parasitic protozoa. All the best to you Felice in California, but do not forget us, we will all miss you.

Jeffrey Hoon Kim

presented by Sidney Strickland on behalf of Sean F. Brady

A.B., Princeton University
Natural Product Biosynthesis in Uncultured Bacteria

Jeff received his undergraduate degree from Princeton and then, after a number of years out of science, he joined Tarun Kapoor's laboratory here at Rockefeller as a technician. Tarun nurtured Jeff's interest in science and while in his lab Jeff developed extraordinarily broad scientific interests. After a couple of years with Tarun, Jeff chose to continue his scientific career as a Rockefeller graduate student. Once in my lab Jeff continued his broad scientific interests and sampled a large number of different projects. He eventually settled on developing a solution to a key problem in our field, the assembly of small overlapping DNA fragments isolated from the environment into functionally accessible larger DNA fragments.

A single gram of soil contains thousands of unique bacterial species, of which only a small fraction is easily grown in the laboratory. The analysis of DNA extracted directly from environmental samples has the potential to provide functional access to genes and gene clusters found in the genomes of these previously inaccessible bacteria. One of the challenges of this approach has been that many gene clusters are too large to be readily captured on a single fragment of DNA cloned from the environment. Traditional methods for the assembly of larger DNA sequences from smaller overlapping fragments were inefficient and technically challenging. Jeff worked out a general experimental framework that permits the reassembly and functional analysis of large gene clusters from smaller overlapping soil-derived DNA fragments using transformation-associated recombination in yeast. The development of practical methods for the rapid assembly of large soil derived gene clusters is an important step toward being able to functionally study metabolites produced by as-yet-uncultured bacteria.

Since leaving Rockefeller almost a year ago, Jeff has moved on to the biotech world and we wish him well in what lies ahead there.

Adria Claire Le Boeuf

presented by A. James Hudspeth

B.A., University of California, Santa Barbara
The Role of the Stereociliary Glycocalyx in Hair Bundle Cohesion

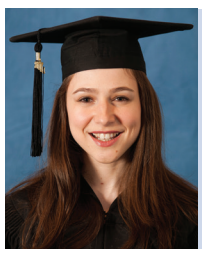
An opera singer can shatter a champagne glass by singing, not only loudly, but at considerable length. The energy delivered by the singer's vibrating vocal cords flows through the air as molecular vibrations that are captured by the glass. Just as gently pushing a child's swing gradually produces enormous oscillations, so the continuous accumulation of sound energy by the glass finally drives it to the point of destruction.

The sensory receptors in our ears work much like miniature champagne glasses. Each receptor — called a hair cell — extends from its top surface a cluster of tiny bristles called a hair bundle. When stimulated by sound, the hair bundle vibrates back-and-forth, gradually accumulating energy and converting it into an electrical form that the brain can interpret.

Although a champagne glass vibrates perfectly well in air, it could not accumulate sound energy if it were immersed in a viscous liquid like water. A hair cell, however, somehow operates in the liquids that bathe the inner ear. In her doctoral research, Adria Le Boeuf explored the physical basis for the hair cell's ability to resonate under water. She found that the tiny bristles of a hair bundle are not simply smooth cylinders; instead, each is coated with a so-called glycocalyx, a thick layer of sugary proteins. This coating in effect lubricates the hair bundle, allowing it to vibrate smoothly even at the very highest frequencies that we can hear, up to 20,000 vibrations per second.

Adria's success in graduate research has been a credit to her determination, perseverance and growing technical prowess. Although she joined us with experience primarily in evolutionary theory, she undertook a series of rigorous biophysical experiments using complex equipment and analytical techniques. In the end, her greatest success came in novel experiments of a design that she developed herself.

Because she has a strong interest in animal behavior, Adria has initiated postdoctoral research in the department of ecology and evolution at the University of Lausanne. There she is investigating how the olfactory repertoire of an ant changes with its employment status throughout life. An individual ant may progress from tending eggs and larvae to working on the nest to foraging abroad for food. In each of these roles the ant must respond to distinct chemical substances. Adria hopes to learn how the switching on and off of particular genes shapes an ant for these various duties.



Geulah Livshits

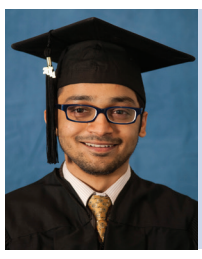
presented by Leslie B. Vosshall on behalf of Elaine Fuchs

B.S., Brandeis University
Rapid Functional Dissection of Genetic Networks via RNAi in Mouse Embryos

I'm truly sorry that I cannot be present today to celebrate the graduation of my student, Geulah Livshits. Geulah was an undergraduate at Brandeis University with nearly straight As. During the summers, she worked at Sloan-Kettering in the lab of Robert Fisher, who indicated what I would soon learn for myself, and come to appreciate — that "Geulah is a real gem."

The name Geulah is the Hebrew word for "redemption," and in this regard, Geulah has been true to her name. Building upon a failed early experiment, in which she had tried unsuccessfully to knock down genes in skin organ cultures, Geulah turned observation into a Ph.D. thesis. She used the information to revolutionize functional studies in mice by devising a noninvasive method to efficiently knockdown genes in live embryos. While my previous graduate students took several years to analyze a gene's function, Geulah managed to accomplish this in a matter of days. This has given Geulah a lot of extra time to think and reflect deeply on the science that she does, and to ask insightful and important questions. She's applied her pioneering discovery to uncovering how mutations in an intercellular adhesion protein, α-catenin, can lead to epithelial cancers in humans, ranging from ovarian to lung to skin cancers. Her work opens the door to the promise for new and improved treatments for some of the world's most common and devastating types of cancers. It also has opened the door for a very promising and exciting future for Geulah as she now continues in her academic career in science.

So Geulah, it has been such a pleasure for me to serve as your adviser through your journey to discover something new, make a valuable contribution to science and complete your Ph.D. thesis. Congratulations on your graduation today.



Tapan Apurva Maniar

presented by Cori Bargmann

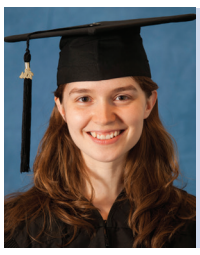
B.A., Bard College
Regulation of Polarized Protein Transport to Axons Versus Dendrites and Sensory Cilia in Caenorhabditis elegans *Neurons*

Tapan Maniar ascended to the highest level of recognition as a high school student, when he won the Indian National Figure Skating Competition, pairs division. These were roller skates, as ice skates are incompatible with the climate. In learning about this historic event, I have learned that figure skating is, in fact, the perfect preparation for a Ph.D. Figure skating demands accuracy, control and intense concentration — traits that Tapan demonstrated in his thesis work, where he addressed fundamental questions about the cell biology of neurons. Tapan labeled specific proteins in the axons, the sites at which neurons send information to their partners, and in the dendrites, which receive information. With accuracy, control and intense concentration, he sought genes required for the segregation of proteins into these different domains.

Candidates in free skating are scored based on their creativity, technical agility and virtuosity. Exactly these qualities allowed Tapan to understand the genes that affect axon and dendrite protein sorting. Clever genetic experiments let him trace a path from proteins in the axon, to the kinesin motor that delivered them, to the microtubule tracks that the motor travelled on, to the function separation of the neuron into signaling and receiving domains.

In the pairs division, the symmetry of the skating performance is an essential element of success. Tapan's thesis work has a pleasing symmetry. In a second project, he discovered how receptors are delivered to dendrites through novel protein modifications, results that mirrored his studies of sorting to axons.

Two marks are awarded for each skating performance: technical merit and artistic impression. Similarly, in science, we judge the quality of the experiment, and the special flair that a scientist brings to a problem. Tapan's thesis work exemplifies the strength, precision and artistry that skaters and scientists aspire to. It merits a perfect 10.



Catherine Oikonomou

presented by Frederick R. Cross

B.S., Duke University
Studies of the Kinetics of Cell Cycle Processes in Saccharomyces cerevisiae

Catherine Oikonomou's graduate work centered on key issues in control of cell division by the master-regulatory cyclin-dependent kinase. A question of particular interest is how the diverse events of cell division are appropriately ordered. A key hypothesis that had been proposed was that order derived from a series of thresholds being crossed as cyclin-dependent kinase activity gradually rose. This hypothesis was largely based on qualitative observations, and other conflicting ideas were also in the literature.

Catherine undertook to test these hypotheses rigorously and quantitatively. She carried out a program involving highly complex genetics, careful biochemical measurements and quantitative single-cell microscopy that was both scientifically highly informative and aesthetically beautiful. Her results placed the "rising levels" hypothesis on a firm quantitative basis; in addition, her rigorous examination of the system revealed many novel and surprising aspects. These insights are significant in themselves, and further, they form the basis for ongoing investigations in the laboratory.

Catherine is staying on through the summer to press forward with some of these studies; later on, she is currently undecided between further work in science and creative writing. I can certainly say from my experience that she is an excellent scientist, and she also writes well and is very creative. So I expect that either direction will work out splendidly for her.

Grigorios Oikonomou

presented by Shai Shaham

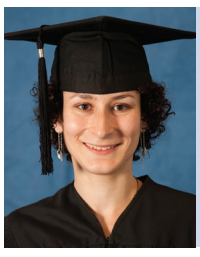
B.Sc., University of Athens
Sensory Organ Morphogenesis in Caenorhabditis elegans

I'm very excited to be here today to partake in Grigorios's graduation ceremony. While in my lab, Grigorios interpreted, united and modified two related quips: He demonstrated, on one hand, that size *does* matter; on the other hand, he showed that bigger is *not* better. And no, Grigorios was not studying animal mating behavior. Rather, Grigorios sunk his teeth into two other very important problems, about which little had been known: How do sensory organs, which allow us to receive information from our surroundings, form, and how are their sizes controlled?

Organ formation is a major unsolved problem in biology, and although technology points us down clearer and easier paths towards making cells of defined characteristics — be they neurons or muscles — how cells are put together in just the right way to make things work remains essentially a mystery. Grigorios addressed the issue of how one component of sensory organs, the glial cell, ensheathes sensory neurons in just the right way to allow a functioning organ to form. Along the way he showed that neurons and glia communicate to arrive at proper organ dimensions, and that glia have proteins that can drive both expansion and contraction of sensory organs, and that it is the balance of these forces that is required to make an organ of the correct shape. Bigger glia, in this system, are no good — sensory organs don't work. Smaller glia don't work either. It is the *right* size that matters.

Grigorios's path in the lab, from my perspective, was exciting, successful, yet uneventful. Grigorios, I think, would paint a different path: one punctuated by deep valleys of despair and towering mountains of accomplishment. And both perspectives are accurate. There is a famous Talmudic saying about life, attributed to Rabbi Akiva, which goes something like this: "Everything is predetermined, but freedom of will is given." One interpretation of this contradiction is that life is a matter of perspective. What Grigorios has done, I think, is to realize this, and for that he has milked graduate school for its purpose — he has learned how to think and appreciate perspective.

Grigorios is going on to study sleep in zebrafish. I know I usually gain the most perspective in my sleep, and I will be closely following his work.



Margherita Peliti

presented by Shai Shaham

Laurea, Sapienza University of Rome
Maîtrise, Ecole Normale Superieure
The Long-range Directional Behavior of the Nematode Caenorhabditis elegans

I am thrilled to be here today to present Margherita. Today is an important milestone in Margherita's career and is a testament to her persistence and strength in the face of many and varied challenges.

Margherita's graduate experience reminds me of a painting by Escher, where one is initially drawn to the dominant shapes or objects within the painting, only to realize that in their spatial arrangement, these create objects similar to themselves. Margherita's studies are in many ways reminiscent of the path she followed during her studies. Margherita's work is like her work. Confusing? Let me quickly explain.

Margherita came to me a few years ago, long after completing a rotation in my lab, and asked whether she could study how the nematode *C. elegans*, a tiny soil worm my lab studies, navigates its environment in the absence of food or other directional sensory cues. Think of a blindfolded person lost in the desert. How would they move around? Could they navigate?

By virtue of studying this problem, of course, Margherita was embarking on a similar exercise. Navigating blindly a question whose answer is unknown, trying to establish a direction, Margherita found something extraordinary. In the absence of sensory cues, worms move in convoluted local paths, perhaps what you might expect of the blindfolded person in the desert. However, even though local movement is meandering, motion in large scale is usually remarkably directional. This result mimics Margherita's graduate research path. Although locally, at small time scales, Margherita constantly battled seemingly disconnected pieces of information, over the course of her thesis, these all fit into a beautiful, vectorial, if you will, story.

To carry this analogy further (if I can be indulged), it turned out that a useful way to examine path directionality of worms employed methods commonly used in a branch of mathematics dealing with objects called fractals, which look the same at all scales. Thus, Margherita and her work, perhaps — different magnifications of the same fractal.

How, you may ask, do worms perform such a navigation feat, which, it turns out, the blindfolded person on their own cannot? We do not know, but Margherita has found some hints, setting up a very interesting problem for her successors to navigate within. How, you may then ask, do scientists navigate a novel problem to illuminate it? If we could easily prescribe such a path, then perhaps graduate school would cease to be the experience that it is.

Maurizio Pellegrino

presented by Leslie B. Vosshall on behalf of herself and Marcelo O. Magnasco

B.S., M.S., University of Turin
Structure-function Analysis of Insect Olfactory Receptors

Maurizio Pellegrino hails from Torino in the Piemonte region of Italy and has been a great colleague and incredibly effective scientist in my group. Maurizio received his laurea degree from the University of Turin in 2004. Before joining my lab, Maurizio published several papers with Marcelo Magnasco on software to correct errors in microarray chips.

In my group, Maurizio became interested in the problem of insect olfactory signal transduction and how this is perturbed by the insect repellent DEET. This was and continues to be a somewhat controversial area and Maurizio contributed important data to the idea that these proteins are odor-gated ion channels distinct from the Buck and Axel vertebrate odorant receptors.

Part of this work was done with collaborators in Tokyo, and we took every opportunity to meet as a group to discuss the project, including scientific meetings in Florida and Honolulu. At both of these tropical beach venues, Maurizio came with his laptop, spent hours discussing the paper and the figures, and flew back to New York to finish more experiments rather than lingering for a vacation. His body of work includes published *Nature* and *Science* papers, a paper we resubmitted to *Nature* yesterday, and two papers still in the works.

As a person, Maurizio is just eerily nice: always in a good mood, always willing to help, with a balanced approach to science and life. In honor of his achievements, Maurizio was named the 2008 David Rockefeller Graduate Fellow. Last August, Maurizio joined the group of Diana Bautista at the University of California, Berkeley, where he is working on mechanisms of touch and pain sensation and by all accounts continuing to be eerily nice and extremely effective.

Andrea Geoghegan Procko

presented by Frederick R. Cross

B.S., Iowa State University
Mitotic Exit: Thresholds and Targets

Andrea Procko's graduate work concerned transcriptional regulation at a key point in the cell cycle, the mitotic exit transition that a cell undergoes as it completes mitosis and becomes a newborn cell. Andrea's experiments were careful, thorough and insightful. As with many biological systems, mitotic exit is annoyingly redundant in its control (at least, it's annoying for the researcher), but Andrea kept her head and carried out all the multiple genetic tests needed to disentangle regulatory control, and she generated many new insights into this complex and important cell cycle step.

In addition to this significant work, Andrea showed herself to be an outstanding team player — she was always willing to set aside her own work to help out a coworker, whether carrying a key experiment needed to make a case, or carrying a partially finished project to completion and publishability after the initial investigator left the lab. This extremely helpful and cooperative attitude is a key feature that has made it great to have Andrea in the lab. She is planning further scientific work, combined with learning teaching skills, since she hopes to focus on the teaching profession in future. I think that her scientific acumen, her highly cooperative and helpful nature and her general all-around agreeable personality all suit her admirably for this goal.

Jonathan E. Schmitz*

presented by Vincent A. Fischetti

A.B., Princeton University
M. Phil., University of Cambridge
Expanding the Horizons of Enzybiotic Identification

A bacteriophage, or phage for short, is a virus that infects bacteria. There are about 10 million phages per gram of soil or milliliter of water, so recent estimates predict that there are approximately 10^{31} phage on earth, the most prevalent biological entity on the planet. To better understand what 10^{31} really means, if you stack each one of these viruses on top of each other, to get to the top of the stack you would have to travel the speed of light — 186,000 miles per second — for 100 million years.

When phages infect bacteria they replicate for about an hour, at which time they need to exit the bacteria to release their progeny phage to infect other bacteria. They exit by producing an enzyme called lysin that drills holes in the bacteria causing them to explode and die. Our lab was the first to successfully develop purified forms of these enzymes for therapeutic purposes. Jonathan was interested in identifying new lysins that would efficiently kill certain disease bacteria. To do this he needed to isolate phage found in the environment. Until Jonathan came along, we isolated lysins by identifying a single phage of interest and cloning the lysin gene from its genome. But with 10^{31} phage out there Jonathan was too impatient to look at one phage at a time, so he developed a metagenomic method by which he could screen the lysins millions of phage at a time.

To do this he needed environmental samples. Water was obvious, and so was soil, but Jonathan wanted an environment with the best potential of finding phage that killed pathogenic bacteria — and that environment was animal droppings. You could imagine that some days in the lab this was very smelly work. There was one memorable trip to the Long Island Game Farm in which Jonathan and other members of the lab, with buckets in hand, collected poop from animals such as lions, tigers, giraffes and zebras, in order to iso-

late the phage and the lysin genes they contain. These genes were then cloned and screened for their killing activity against the disease bacteria in question.

Jonathan was very successful in this endeavor. Using the method he developed he identified many new lysins directed to some of our most deadly pathogens. One of the lysins he identified is directed to methicillin resistant *Staphylococcus aureus* or MRSA, the organism responsible for more than 700,000 major infections in hospitals and the community. This lysin has now been licensed by a biotech company and is being developed to prevent and treat MRSA infections.

In his spare time, of which there was very little, Jonathan met Francesca, a lovely Italian scientist who he married about two years ago. Jonathan's current interests lie in pathology and he will be going to Vanderbilt University on a pathology fellowship as part of the M.D.-Ph.D. program.

Jason Schwarz

presented by A. James Hudspeth

B.A., University of Pennsylvania
A Hydrodynamic Sensory Antenna Used by Killifish for Nocturnal Hunting

Humans have four important senses: vision, hearing, touch and taste. We can also smell. But other animals live in quite different sensory worlds owing to their physical environments and lifestyles. For instance, bats and whales hunt by the use of sonar: they navigate and follow their prey by bouncing acoustic signals off their surroundings and analyzing the resultant echoes. Pit vipers such as the rattlesnake can visualize their warm mammalian prey in complete darkness by use of infrared sensors. And birds, bugs and bacteria can use magnetic senses to regulate their migrations.

Jason Schwarz brought to our group a strong interest in ethology, the study of animal behavior. He focused his attention on a particular type of fish, a killifish or topminnow, that hunts mosquito larvae on the water's surface. The fish is so effective that it can rapidly pick off these targets from a distance of several inches and in total darkness. How might a fish detect such creatures? Each time a larva moves, it sets up miniscule ripples that propagate a short distance across the water's surface. An elaborate array of sensory receptors on the killifish's head detects those ripples and somehow informs the fish of their source.

Jason showed that the receptors in question are highly directional: each part of the sensory system acts like a tiny antenna pointed in a particular direction. Just as we can use electronic antennae at different positions to determine the source of radio waves by triangulation, so the fish uses inputs from several of its receptors to ascertain the location of its target.

Having now moved to Stanford University School of Medicine, Jason is continuing his work at the interface of ethology and neuroscience by studying the neural basis of attention. All of us can concentrate our vision on a particular target in space, and by so doing enhance our ability to discern fine details. This focusing of attention does not occur inside the eyes, but rather in the representation of visual space within the brain. Jason is seeking to understand the nerve cell activity that underlies concentration in the chicken. Although this creature is not renowned for its mental ability, it is a readily accessible, hardworking and uncomplaining experimental subject that has proven capable of directing its attention to the most important things in its life, namely grain, grain and still more grain. It is a surprise that a chicken can pay attention to anything, but it will not be a surprise if Jason can figure out how.

Matthew Sekedat

presented by Brian T. Chait

B.S., Michigan State University
A Proteomic and Genomic Investigation into the Dynamics of DNA Replication

A central requirement of any living system is its ability to make virtually perfect copies of itself. To do this, it is necessary that living cells faithfully replicate their genetic material. If this does not happen properly, bad things can happen to an organism including, for example, the onset of cancer in humans.

Matt Sekedat's research concentrated on developing new tools for following the intricate dance of the macromolecular actors that bring about DNA replication during the life cycle of a cell — using as his model system that old friend of biologists and beer drinkers, brewer's yeast. The tools that Matt developed during the course of this work proved extraordinarily powerful, allowing him to investigate the detailed dynamics of DNA replication through the cell cycle, and in the process providing the field with intriguing new insights into the replication process.

Prior studies in brewer's yeast had led to a picture wherein the replication of DNA progresses at variable rates over different parts of the genome, pausing at numerous sites along the way. These data were interpreted to mean that the dynamics of replication progression are strongly affected by local chromatin structure or architecture, and perhaps by interaction with the machineries controlling transcription, repair and epigenetic maintenance. Matt's results, which measured the genome-wide dynamic replication processes with unprecedented accuracy and resolution, provide a very different picture. He demonstrated that the replication machineries progress at remarkably uniform rates regardless of genomic location. This finding was surprising given the prior results that dominated the field for more than a decade, and has led to a substantial revision of our view of this very fundamental process. Indeed, Matt's beautifully executed experiments show that the dynamics of the replication fork in budding yeast is simpler and much more uniform than was previously recognized.

Scientific explorations of this sort have much in common with expeditions into unknown and sometimes dangerous territories. Given Matt's extraordinary patience, creativity and absolutely first-rate judgment, I can think of few that I would prefer to have as a companion on such an expedition. I count myself very lucky to have had such a talented and stimulating expedition companion.

Alice O. Kamphorst Silva

presented by Michel C. Nussenzweig

B.S., M.S., Universidade Federal de Minas Gerais
Antigen Presentation: Influence of Cell Type and Route of Antigen Uptake

Alice O. Kamphorst Silva is originally from Brazil. Although her parents are both in physics and mathematics, she chose to study biology and received an undergraduate degree in Minas Gerais before coming to Rockefeller for her Ph.D. In Minas, Alice had studied with Nelson Vas, an immunologist who has spent quite some time here in the U.S. and is an inspiring teacher. So when she came to Rockefeller, she knew that what she wanted to study is how the immune system distinguishes between self and non-self and how it maintains tolerance. In addition, Alice was one of those students who arrives and does not have to be taught how to do experiments.

So I gave her an exceedingly difficult project on which even she struggled with but managed to excel. For her thesis she explored the properties of different types of immune cells in presenting different types of antigens. She established the relative contribution of closely related dendritic cells and macrophages to this process. Alice's work was published in *Science* and the *Journal of Immunology*.

Alice is a real Brazilian, with an outgoing and sunny personality, and she even dances capoeira, which is a beautiful fluid mixture of dancing and martial arts. For her postdoctoral fellowship, Alice has joined the laboratory of Rafi Ahmed at Emory University, where she continues to work on immunology and vaccine development.

Clare Walton

presented by Fernando Nottebohm

M.Biochem., Exeter College, Oxford University
Net Addition and Long-term Survival of Adult-born Neurons in the Zebra Finch HVC

Clare Walton came to Rockefeller from undergraduate work at Oxford, where she had studied biology. I suggested to her a thesis project, but it proved to be unworkable. While finding this out, however, Clare observed that the packing density of neurons in a part of the song system of zebra finches continued to grow in adulthood, well after song was learned, leading to an eventual doubling in the number of neurons in that region. As time went by these neurons became smaller and more densely packed. This was a novel consequence of adult neurogenesis, because in previous instances the addition of new neurons in adulthood had been accompanied by either replacement of existing cells or a net gain in volume of the part of the brain that received them.

Clare has shown that the addition of new brain cells to the adult brain can have a diversity of outcomes, none of which was predicted or required by the present understanding of brain function. Her thesis work is innovative, radical and delightful and as of today, we do not know how the doubling of neurons that she observed affects what the brain can do. Discoveries that do not make sense are usually good harbingers of future progress.

Clare will soon go to Australia to study bird behavior in the field.

John Paul Wilson

presented by Sidney Strickland on behalf of Howard C. Hang

B.S., B.A., Oregon State University
Bioorthogonal Chemical Reporters Reveal Fatty-acylation of Histone H3 Variants and Directly Image Cholesterol on Proteins and in Cells

I am pleased to present John Wilson with a doctorate of philosophy from The Rockefeller University today. My laboratory is generally interested in developing new chemical methods for investigating the role of protein modifications that are important for microbial pathogenesis. John was the first graduate student that joined my laboratory when I started at Rockefeller in the beginning of 2007.

When John started, the lab was just a room of empty benches. John and another postdoctoral fellow were instrumental in setting up the laboratory, for which I am very grateful. After getting the lab up and running, John's thesis work focused on developing a biochemical method of identifying novel fatty acid-modified proteins from mammalian cells. Lipid modifications provide important temporal and spatial regulation of protein function in membranes, but have historically been difficult to analyze biochemically. Through the application of lipid chemical reporters and proteomic methods, John was able to develop a robust method to biochemically identify new lipid-modified proteins in mammalian cells.

John's thesis work suggests that many more proteins may be regulated by fatty acid-modifications than previously appreciated. Notably, John's studies identified a potential site-specific lipid modification of histone H3 variants, nuclear proteins that are key components of chromatin involved in regulated gene expression. This discovery was unpredicted and a complete surprise that sparked many questions about the potential functions of histone H3 lipid modification for future studies. These studies culminated in a nice publication in *Molecular and Cellular Proteomics* where John is first author. I thank John for his contributions to getting my lab started and congratulate him on a terrific Ph.D. thesis.

Coming soon, to The David Rockefeller Graduate Program

As the class of 2011 prepares to move on, a new batch of graduate students is set to take their place. Rockefeller's application screening committee pored over 797 applications of potential new students this year, eventually winnowing the list down to 93 acceptances. Of those, 30 have enrolled in The David Rockefeller Graduate Program this fall and one has deferred admission until 2012.

The 2011 entering class includes 17 men and 13 women from seven countries: Albania, Austria, Mexico, the Netherlands, Singapore, Turkey and the United States. Their alma maters include: Augusta State University, Ball State University, Bilkent University, Cornell University, Fordham University, Hunter College, Indiana University of Pennsylvania, Karl Franzens University, Kenyon College, Linfield College, National Autonomous University of Mexico, New York University, Saint John's College, Spelman College, Texas Christian University, Tufts University, University of Amsterdam, University of Arizona, University of Chicago, University of Illinois, Urbana–Champaign, University of North Carolina, Chapel Hill, University of Pennsylvania, University of Rochester, University of the South, University of Wisconsin, Madison and Yale University.