BenchMarks

THE COMMUNITY NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

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Convocation 2005

PHOTO: BRUCE GILBERT

For the 22 Rockefeller graduate students who received Ph.D.s this year, June 16 was the culmination of over 100 years of combined study and laboratory work. The celebration in their honor was a daylong affair, which included a formal luncheon, a procession across the campus, a degree ceremony presided over by President Paul Nurse and Board Chair Russ Carson, and an evening of drinks and dancing in Weiss Café.

The class of 2005, the first to graduate from the newly named David Rockefeller Graduate Program, consists of 13 men and 9 women who hail from 10 foreign countries — Cyprus, England, Estonia, Italy, Germany, Japan, Malaysia, Mexico, Peru and Slovenia — as well as the United States. Their future plans include postdocs, industry jobs and medical school.

"This year's graduating class is superb, and I'm confident they'll carry on the great tradition of Rockefeller's previous 873 graduates, who are world leaders in research, academics, business and other fields," said Dean of Graduate and Postgraduate Studies Sid Strickland, in comments at the luncheon.

Here, we present our annual Convocation issue, a tribute to Rockefeller's newest generation of scientists.

CELEBRATING 100 YEARS · 1901 · THE ROCKEFELLER UNIVERSITY · PRO BONO HUMANI GENERIS

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Chad Euler awarded David Rockefeller Fellowship

BY STELLAR KIM

After stints as an improv actor and beermaker and a month-long solo hike on the Vermont Long Trail, Chad Euler came to Rockefeller in the summer of 2002 and went right to work in Vincent Fischetti's lab. He never turned back.

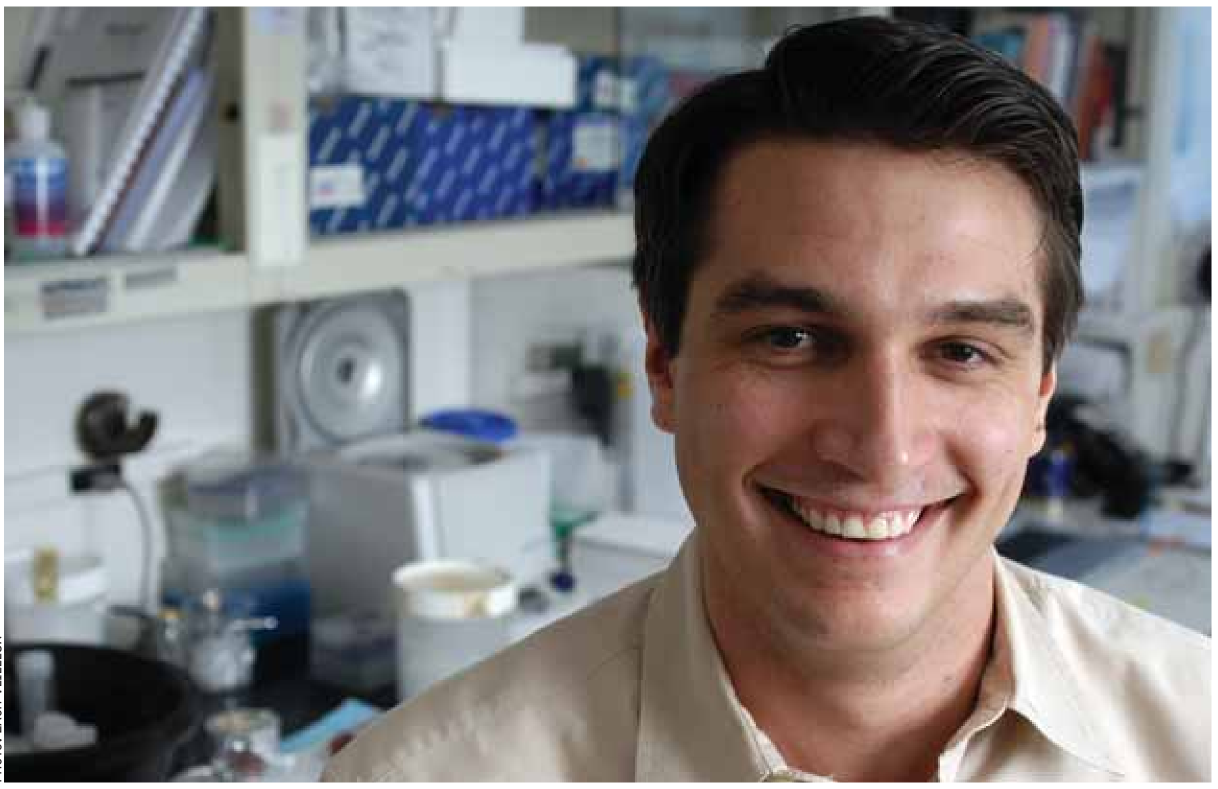


PHOTO: ZACH VEILLEUX

"I always say you have to work really hard and enjoy life to an equal extreme," Mr. Euler explains. According to Dr. Fischetti, Mr. Euler is an exceptionally hard worker who came to the lab several weeks early and doubled up on classes to spend more time on his research. He's also been an active member of his community, serving on committees and helping with recruitment of prospective graduate students.

For those who know him, then, it was no surprise when it was announced that he would receive the David Rockefeller Fellowship this year, an annual prize that recognizes exceptional scientific and leadership promise.

Mr. Euler is studying how bacteriophages, viruses that infect bacteria, influence the type and severity of disease caused by the pathogenic bacterium *Streptococcus pyogenes*. Best known for causing strep throat, *S. pyogenes* is responsible for a variety of infections, including scarlet fever, streptococcal toxic shock syndrome and flesh-eating disease. Mr. Euler is looking specifically at the roles that lysogenic or DNA-integrated bacteriophages play when people first come into contact with *S. pyogenes*. His research focuses on the impact of specific bacteriophage genes on streptococcal colonization, spread and survival.

"I enjoy problem solving," Mr. Euler says to explain his interest in microbiology. "Since I was a child, I was always asking why. Why things work the way they do and what's going on under the surface. Being a student at Rockefeller means I can make good use of my curiosity."

Originally from Maryland, Mr. Euler studied microbiology as an undergraduate at the University of Vermont, where he focused on molecular genetics. After a yearlong job at a pharmaceutical company preparing medication for clinical trials, he joined the Magic Hat Brewing Company to head up quality control for the upstart microbrewery. Later, returned to academia, working as a research technician in the immunobiology department at the Yale Medical School. Between professional pursuits, Mr. Euler hiked 270 miles from Canada to Massachusetts and battled Hurricane Floyd, which sent wet trees falling down in his path. "I had to drain my boots a lot," he says, "but it was great."

He chose to attend Rockefeller because of its generous support of students. "At other schools, students have to form unions and fight for basic things like good health care coverage," he says. "Here, there's open dialog among the students, faculty and the administration. Being a student here is a lot like being a postdoc somewhere else."

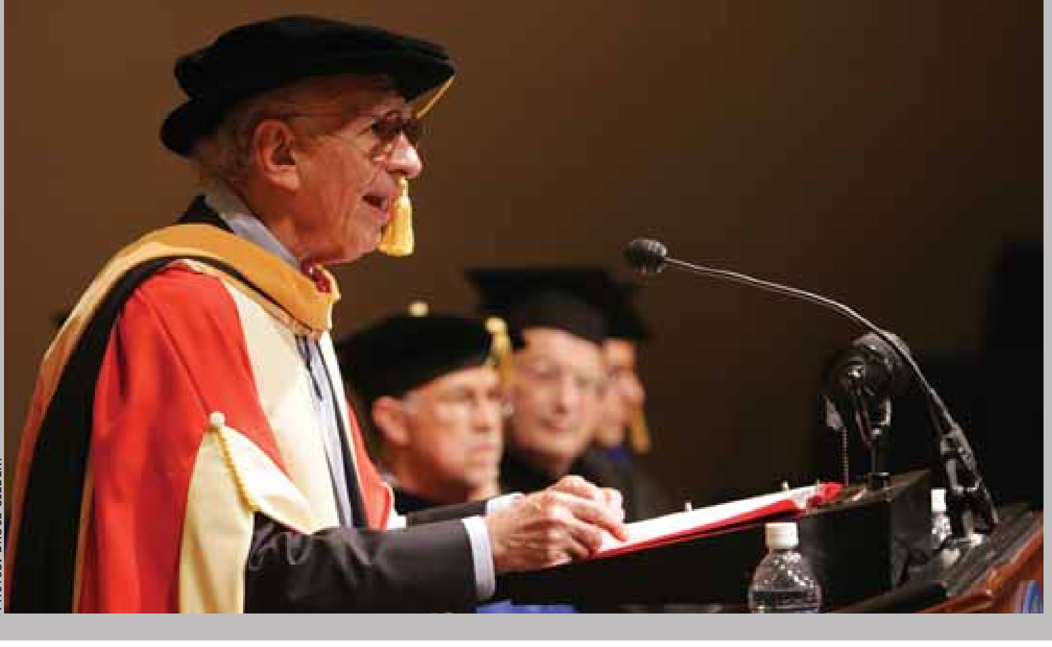
Enthusiastic about student involvement, Mr. Euler has served for two years on the Student Representative Council, is an advisor to the Student and Faculty Club board of directors, and helps during the prospective student open house each year.

And he's been impressed by his classmates. "They are good scientists who can also function in the real world and who have diverse interests and skills," he says. "There is a true sense of a community at Rockefeller. People are united toward a common goal, which is to ask and answer questions."

Mr. Euler says he plans to pursue his postdoctoral work in research involving disease. Although he is uncertain whether he will eventually work in the biotechnology industry or academia, he is certain his days will be spent in labs. He also wants to coach soccer and lead children on camping trips.

Since 1998, the David Rockefeller Fellowship, which includes a monetary award, has been awarded to an outstanding third-year student who demonstrates exceptional promise as a student and leader. "It really excites me to be given this great honor," Mr. Euler says. "It's great validation. When people are interested in your research and care about you as a student, it motivates you to be a better scientist and to pursue what you're doing with passion and conviction."

Eric Kandel, David Sainsbury receive honorary degrees



PHOTOS: BRUCE GILBERT

As is tradition, each year the university awards one or more honorary doctor of science degrees to scientific leaders who have made extraordinary contributions in their fields. This year the honorary doctorates, which are the most distinguished awards the university makes, went to neurobiologist Eric R. Kandel of Columbia University and Great Britain's science minister Lord David Sainsbury.

Dr. Kandel *(left)* was a trustee of Rockefeller University from 1995 to 2001 and is today a trustee emeritus and a member of the Board's Committee on Scientific Affairs. He majored in history and literature at Harvard College but, influenced by a fellow student and fellow Austrian, became interested in psychoanalysis. He attended New York University Medical School and continued his training at the National Institutes of Health and the Institut Mornay in Paris. He joined the faculty of New York University and, in 1974, left to found the Center for Neurobiology and Behavior at Columbia.

"Eric's studies have been pivotal in relating three psychologically defined forms of learning — habituation, sensitization and classical conditioning — to subcellular process and intercellular signaling," Paul Nurse said at the June 16 Convocation ceremony. "He has shown that simple behaviors can be accounted for by distinctive sets of nerve cells connected in invariant circuits and that learning produces changes in behavior not by altering basic circuitry, but by adjusting the strength of particular connections between the nerve cells."

Lord Sainsbury *(right)*, although initially also a history student, transferred his major to psychology because of a fascination with the breakthroughs being made in the study of DNA. He graduated from Cambridge and went on to earn an MBA from Columbia University, then joined his family's supermarket business and rose to become finance director, then chairman and chief executive. In 1998 he stepped down from these private posts to become UK Parliamentary under-secretary, with responsibility for the Office of Science and Technology, Research Councils and space matters. He was also named science minister in Prime Minister Tony Blair's administration and became a member of the cabinet biotechnology committee, Sci-Bio, responsible for national policy on genetically modified foods.

"David's passion for science is equally evident in his philanthropy," Dr. Nurse said. "He established the Gatsby Charitable Foundation in 1967, when he was 27 years old, using his own inheritance, and the foundation has given unparalleled support to the study of plant genetics, and genetically improving the resistance of plants to disease. It has also fostered research in cognitive science."

For transcripts of the remarks made by Dr. Kandel and Lord Sainsbury, please see www.rockefeller.edu/benchmarks.

Rockefeller's *other* graduation

A LARC program that teaches adult high school students to become animal caretakers honors its second successful class

BY STELLAR KIM

It's a little known fact, but not everybody who studies at Rockefeller University is laboring toward a Ph.D.

Last month, in a quiet ceremony held on the third floor of Weiss, 12 high school students from the Manhattan Comprehensive Night and Day High School (MCNDHS) celebrated their graduation from a program, cosponsored by Rockefeller, that trains high school students to become caretakers for laboratory animals.

"I never thought I'd be doing this," Wendy Cordova, a high school student working as an animal care technician at The Rockefeller University's Laboratory Animal Research Center (LARC), says of her 10-month internship. "Since I got my first cat at 11, I knew I wanted to do something with animals. I never knew there were these kinds of jobs," she comments. The Laboratory Animal Science Program here helped Ms. Cordova transform her general interest into new career goals.

Now in its second year, the Laboratory Animal Science Program selects students with strong interests in science, and prepares them for national certification as laboratory animal technicians. Over the course of the school year, students from MCNDHS, a unique public high school on Second Avenue near Union Square, come to LARC to learn about husbandry techniques, animal handling, research practices and laboratory safety. The students work alongside LARC's 75 animal attendants and technicians.

PHOTO: ZACH VEILLEUX

Animal house. Christopher Ariza and Sylwia Muratovic, graduates of a program that trains adult high school students to become laboratory animal caretakers, in one of the LARC rooms where they received training.

This program supports the university's attempts to engage high school students in the sciences, and it generates interest in the important work of providing healthy, humanely maintained laboratory animals that are essential to quality biomedical research. It also creates a pool of employable animal technicians from which Rockefeller — and other city animal facilities — can hire. To help place this new crop of skilled technicians in laboratories, the program staff helps students apply for jobs, reviewing their resumes and organizing job fairs that bring major New York City hospitals to the campus. Many of them will stay on to work at LARC.

Fred Quimby, associate vice president and senior director of LARC, stresses that the internship doesn't just teach the mechanics of lab technique, it also gives students a taste of the discipline and teamwork required of laboratory workers. It also instills in them a respect for the rigors of science. "The sense that they can be involved in scientific research is incredibly empowering," he says.

"You learn here what you can't outside," says Stanley Bonnefil, a graduating student. "Here, one mistake can lead to disaster. Everybody has to do their job and help each other." Mr. Bonnefil says this program has exposed him to a different level of opportunity in science. Though he'd previously held science-related jobs, including a stint as a guide at the Hall of Science Museum, he now has aspirations of becoming a heart surgeon. "Here I get to do the science, not just explain it," he says.

For the students, who are between 17 and 21 and in many cases have had their educations interrupted by personal events or immigration, the opportunity can be life-changing. "The bar is raised for them. They're given new academic challenges, professional responsibilities and new goals, and when they meet these expectations, it's such a sense of accomplishment," says Bonnie Harwayne, MCNDHS's head guidance counselor. The program accommodates work or family obligations by offering some classes during the evening.

From last year's class of 16 students, 11 continue to work in LARC. Some, like Jonathan De Jesus, credit the program with instilling a sense of focus and discipline in his life. "I know what I want now and it makes no sense not to go for it," Mr. De Jesus says. He has already applied for a promotion to group leader and in January he plans to enroll in college.

With a stable career, he says he is also ready to marry this year. "Things are all falling into place. I never would've imagined any of this two years ago."

New teaching awards program recognizes four Rockefeller faculty

BY STELLAR KIM

Though the Convocation ceremony is largely a celebration of scientific achievement, it's more than pure labwork that gets graduates their hoods. There are also classes.

This year, a new program to recognize the teachers of those classes is raising the profile of the university's coursework. Four faculty members — **Peter Model**, **Nina Papavasiliou**, **Shai Shaham** and **Leslie Vosshall** — who lead the popular "Experiment and Theory in Modern Biology: Methods and Logic" seminar were awarded the first annual Rockefeller University Distinguished Teaching Awards. The awards, which in future years will be presented to one or two instructors selected by a committee composed of the president and scientific vice presidents, consist of a plaque and monetary prize and were presented at the Convocation Luncheon June 16.

"With this award, we will recognize faculty who make a significant impact on the learning community at Rockefeller," says Dean of Graduate and Postgraduate Studies Sid Strickland.

"Experiment & Theory in Modern Biology: Methods and Logic" is one of the only required courses at the university. Dr. Papavasiliou, head of the Laboratory of Lymphocyte Biology, Dr. Shaham, head of the Laboratory of Developmental Genetics, and Dr. Strickland proposed the class three years ago to introduce students to the methods and principles behind current biological research. The course is run as a two-section seminar in which students analyze and discuss seminal papers in scientific research.

The instructors choose papers that have become, as Dr. Papavasiliou calls it, "scientific gospel." One such work is a 1927 article on the transmutation of the gene, remarkable because modern understanding of the gene did not come about until some 20 years later. "This prescient discovery about how something works was made without complete knowledge of the exact nature of that thing," Dr. Papavasiliou explains. "We hope cases like these shape students' fundamental understanding of how science is done; that scientific discovery can be messy and that the wrong experiment can produce the right answers."

Students of the course say it helps put their labwork in a broader perspective, and forced them to question the impact of data presented in papers. "We typically see scientists through their finished product, but in this course, we were asked to look at the way people approach problems and to evaluate their choices and methodology," says Grigorios Oikonomou, a Rockefeller graduate student who recently completed the class.

"It's not enough for Rockefeller to simply train its students to carry out experiments," says Dr. Strickland. "Scientists also need to be innovative and critical thinkers who follow the science where it takes them."

To help foster those skills, Methods and Logic is student-led. Instructors encourage collaboration and open dialog and work to foster a sense of community, but don't give lectures. "What's most important about the class is that not only does it allow the students to bond socially, but it forces them to think critically," says Dr. Vosshall, head of the Laboratory of Neurogenetics and Behavior. "That's something they'll need to do throughout their careers."

Convocation 2005

One of Rockefeller's unique Convocation traditions is the tributes given to graduates by their faculty mentors. Printed here are the transcripts of these speeches, as they were read on June 16. In addition to graduates below, four others — Esra Asılmaz, Eli Chen, Lily Copenagle and Deborah M. Gurner — were awarded degrees in absentia.

For a transcript of the remarks made by Tshaka Cunningham in his student address, please see www.rockefeller.edu/benchmarks.

Ian C. Berke

B.S., Cornell University
Nuts and Bolts of the Nuclear Pore Complex: Nup133 Structure Highlights the Modularity of the NPC
presented by Günter Blobel

The nucleus is the innermost sanctuary of the cell. It harbors essentially all of the cell's DNA. To secure this sanctuary, it is surrounded by a double wall. And that double wall is not impenetrable, however, but has many gates. After all, even a sanctuary has to be constantly supplied from the surrounding environment, in this case from the cytoplasm. Each gate is occupied by a nuclear pore complex that functions like a guard. It controls who gets in and out and to get in and out you need a ticket. The guard, the nuclear pore complex, checks the ticket and allows both for entry and exit. It's sort of like a doorman in a New York apartment building, but the nuclear pore complexes are much busier than the doormen. About a million large molecules, with their corresponding tickets, have to be checked per second to allow traffic in both directions, entry and exit. Occasionally the wrong molecule gets access to the nucleus and this can result in immediate murder. The DNA is degraded and the cell dies. Or of course it can result in molecules getting in whose long-term effects lead to cancer. So this is not just an academically interesting topic, but it is also a topic that is interesting of course for medicine.

The nuclear pore complex is a very beautiful structure. It looks like an octopus with 10 tentacles (of course some of you don't like octopuses) on both the nuclear and cytoplasmic site. Not much is known of its fine structure and no X-ray crystallographic studies had been performed before Ian decided to try his luck. Of course it made no sense to crystallize the entire nuclear pore complex because it's large; it is the largest protein complex in the cell.

But a closer look at the proteins showed that they were really modular in nature. So he went after one of these modules, crystallized it, and solved its atomic structure. This was the first atomic structure of a nuclear pore complex module and is therefore a landmark achievement in structural biology.

Ian was born in Brooklyn and grew up with three brothers in Sheepshead Bay, not far from the ocean and Coney Island. His interest in science was awakened early and encouraged by his parents. He participated at a Westinghouse Science Fair and received an academic all-American award for his activities. He went to Cornell University, where he studied biochemistry, and it is there where he developed his deep interest in structural biology, particularly X-ray crystallography. He then joined Rockefeller University as a graduate student and started his work in Rod MacKinnon's laboratory. In 2003, he joined our laboratory and completed his studies here in less than two years, which is a new laboratory record.

Ian was also productive in his private life. He and his wife are parents of very lively twin girls and they already made themselves known. You heard their lovely voices. I heard them several times in the lab. He is also an initiator of the campus student newspaper and was one of its principal contributors. Ian moved to Cornell in the meantime, where he continues his training as a postdoctoral fellow and where his wife is completing her studies towards a doctor of veterinary medicine.

Mr. Carson, President Nurse, it is a great pleasure to present to you Ian Berke, for the degree of doctor of philosophy.

Andrea Bocci

Universita Di Pisa, Laurea
Neural Network Guided Search for Particle Resonances at Fermilab
presented by Konstantin A. Goulianos

The stated mission of The Rockefeller University is to understand life for the benefit of humanity. In his thesis, Andrea Bocci settles for nothing less than understanding the life of our universe itself.

His goal is to find the Higgs particle, which can be thought of as the quantum of the life force of the universe. The discovery of the Higgs is the main goal of a huge particle accelerator currently under construction in Europe, in which physicists will look for Higgs particles produced and immediately decaying in two jets of ordinary particles. These jets must be sorted out from the debris of several hundred particles produced in each collision, which is a daunting task considering that only one in a trillion events may contain a Higgs.

In his thesis, Andrea is testing a method of optimizing a jet finding algorithm by looking for jets from the decay of W and Z particles, the carriers of the weak force, produced in association with a gamma-ray in proton-antiproton collisions at the Tevatron, Fermilab's proton-antiproton collider. It is like looking for a needle in a haystack. The method is based, appropriately for a Rockefeller student, on a neural network approach, in which about 20 variables in an event are correlated automatically to produce the best possible result. The computer program must be trained to do this job automatically. Andrea spent years training his computer program, and his results are rewarding. He estimates that by using this method the time needed to run the experiment will be reduced from two years to one. This represents tremendous savings considering the $200 million budget and the time of the 1,000 or so physicists involved in running the experiment.

Who is Andrea? Briefly, he graduated from the University of Pisa, and so it is not surprising that he followed the example of the great Galileo in trying to understand the entire universe. If I were to describe him using a single word I would use "quiet." He was involved in everything that had to do with the experiment and with the lab, and everything was done professionally and quietly before you knew it. When he ran the New York City marathon last year, I learned about it only in the last minute. "Just do it" is a motto that was created for people like him. He comes from a small city in Italy, called Recanati, located just opposite Rome by the Adriatic sea, which is the quietest sea that I ever saw. No wonder!

"How far from the sea is Recanati?" I asked.

"It depends on whether you are going to the sea or coming from it," he replies.

"How come?" said I, thinking of traveling by car.

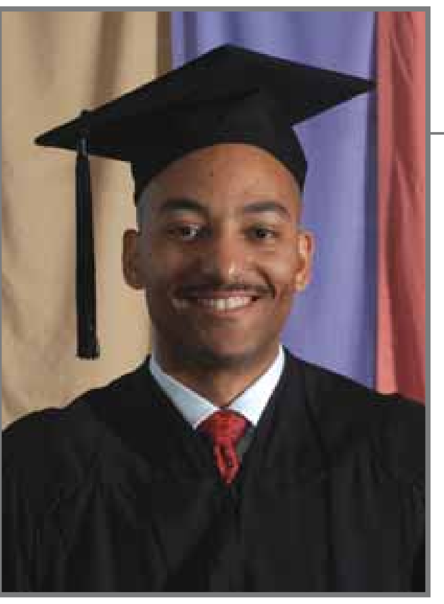
"Well, the town is on a hill, and using a bicycle you can kind of roll down to the sea in 20 minutes, but it takes 40 minutes to come back."

"Oh!"

Mr. President, Mr. Carson and honored guests, it is with great pleasure and personal pride that I present to you Andrea Bocci for the degree of doctor of philosophy.

Tshaka J. Cunningham

A.B., Princeton University
Exploring the Early Events in the HIV-1 Life Cycle: From Post-entry Restriction to Nuclear Import
presented by Mark Muesing



What's in a name? Often in science name recognition plays an important underlying role. After all, science has an aspect of glamour and mystique (almost Hollywood in nature) that, given the same level of scientific merit, those blessed with a unique, catchy name will be remembered for their work with more frequency and with more durability than others. In some cases, in referring to the individual, the name is truncated, the surname dropped altogether and recognition is assured by a single name. For example, Tshaka Cunningham has been favored with a great name. Tshaka, or Shaka, as those close to him abbreviate affectionately, was named after the 19th century south African warrior, Tshaka Zulu, roughly translated into "one worth a thousand." Indeed, I would venture that the majority of those on campus know the name Tshaka straight away, even those without direct interaction. But while name recognition is one thing — it must be coupled with performance and achievement to formulate success.

Shaka's thesis work involves the study of an aspect of HIV-1 biology that may contribute to the covert evasion of the virus within infected individuals as well as have practical implications for the application of gene therapy modalities. HIV-1 belongs to a viral family that has the ability to traverse the cytoplasmic compartment and to gain access to the nucleus of its target cell regardless of whether the cell is capable of cell division. In either cell type, this step, known as nuclear import, is absolutely required for viral propagation. At the end of this process, the genetic information of the virus fuses with the host's chromosomal DNA, thereby making the HIV genome a permanent fixture in the cells of an infected individual. Although the nuclear import of the viral genome is a required step in the viral life cycle, it remains unexplored as a target for antiretroviral therapy. In addition, since HIV can accomplish this step in cells that are non-dividing, understanding the molecular mechanics utilized here may help further the design of viruses in which pathogenic determinants of the virus can be removed yet still be capable of the stable transduction of target cells (for example, stem cells). Thus, over the course of the past few years and in collaboration with other members of my lab, Shaka has discovered that, in addition to its other functions in viral replication, the HIV-1 integrase protein plays the key navigational role in coordinating the passage of the virus into the cell nucleus and has identified a likely cellular pathway it commandeers to do so.

Tshaka has been awarded over his years at Rockefeller. He received the UNCF Merck Award to fund several years of his studies and the prestigious David Rockefeller Fellowship, awarded to a third-year student for scholarship and outstanding contribution to the university. In addition, he was chosen to deliver the commencement address given earlier today, where I might add, he did a bang-up job. Thanks for the kind words, Tshaka.

Finally, I just want to mention at Tshaka's graduation a special person that was close to him during his first years at the university. Jean Devlin, assistant dean of students, who passed away a few summers ago, was a constant champion and friend of Tshaka. I know that if she were with us here today she would be very proud of him and realize that her vision of Tshaka going forward has been fulfilled. Tshaka, as his namesake foretells, is a natural-born world-shaker. We wish for him only the very best in the future.

Mr. President and honored guests, it is my pleasure to present to you, Dr. Tshaka Jawanza Cunningham.

Andrew T. DeWan

B.S., Brandeis University
M.P.H., University of Minnesota
Interpreting the Human and Other Genome Sequences via Computational Methods
presented by Jürg Ott

Andy received his B.S. degree at Brandeis University in 1996 and then worked for two years at MIT in the Center for Learning and Memory of Nobel Prize winner Susumu Tonegawa, where he obtained wet lab experience. After receiving an M.P.H. degree in epidemiology at the University of Minnesota in Minneapolis, he came to this university in the fall of 2000 with the wish to work in my lab and become a statistical geneticist.

Andy was a great student. He interacted with other lab members and did seminal work on the comparison of genetic and physical maps and on the distribution of transcription factor binding sites in the human genome. Before he came to my lab, he had already published six papers and added another seven while working here. He has now accepted a position as a postdoctoral associate with Josephine Hoh at Yale University.

On a more personal level, Andy has a nice temper, is unselfish, and has been very pleasant to work with. Some people may say he is very quiet but, as you might imagine, this is not a trait I consider a disadvantage.

Mr. President, Mr. Carson and honored guests, it is my pleasure to present to you Andrew DeWan.

PHOTO: ZACH VEILLEUX

Volunteers, including Atsuko Horiuchi from the Greengard lab, carry colored banners representing the labs from which students graduated this year.

Marc-Werner Dobenecker

Vordiplom, University of Osnabrück
Diplom, University of Cologne
Great Expectations: Function of the Csk Adaptor Protein Cbp in T Cells
presented by Alexander Tarakhovsky

Marc Dobenecker came with me to Rockefeller from Cologne, Germany, and with very definitive and well-understood Germanic determination tried to figure out how to keep things in order as far as lymphocytes are concerned. And most of his time he spent trying to understand negative regulation of signaling in lymphocytes and how these negative forces maintain lymphocytes away from attacking self and therefore preventing auto-immunity.

I must say that he put in an amazing effort into trying to understand it and he failed and succeeded at the same time. And I can only cite the Russian poet Pasternak, who said that one should not distinguish the failure and success because they both have equal values. And while failing on one side, Marc discovered, together with another member of my lab, a novel post-translational modification in the cytosol that potentially may lead to our better understanding of how cells receive, transmit signals, and interpret them and that may contribute to potentially big discoveries. And while I'm talking about big discoveries, I want to refer to one point of my personal — and somewhat Marc's — history as well.

When I arrived at Rockefeller University, I was gently stopped by a security guard, who asked me where I am coming from, and once he learned I'm from Germany he said, "Oh, there are a lot of Germans here and you know, they come here, stay a couple of years and they'll get a Nobel Prize." So Marc, I'm afraid you're leaving too early.

Mr. President, Mr. Carson, it's a pleasure to introduce Marc Dobenecker: a great man and a good scientist.

PHOTO: BRUCE GILBERT

Tshaka Cunningham *(left)* gets some help with his gown from fellow graduate Marsha Nidanie Henderson.

Noel L. Goddard

B.S., M.S., Polytechnic University
Why this Genetic Code? An Investigation into the Stability and Error Tolerance of the Genetic Code
presented by Sidney Strickland (on behalf of Joshua Lederberg)

As you all know, the information from which each of us is constructed is encoded in the giant DNA molecules that make up our chromosomes. The molecules that compose the fabric of our bodies, though, and the enzymes that do the body's chemical work are proteins that are assembled from amino acids. Every cell of our body must therefore read out the genetic blueprint stored in DNA and use this information to correctly assemble the amino acids that make up some 20,000 different proteins.

The key intermediate step in this process is called translation, an apt name: the information stored in DNA as a string of As, Cs, Gs, and Ts must be translated into another language, that of the 20 amino acids. The dictionary used for this translation is called the genetic code: the specific, consistent, nearly universal association of each three-letter combination of DNA bases with a specific amino acid. The combination "GAG," for example, specifies the insertion into a protein of the amino acid glutamate — the same substance found in the MSG of Chinese restaurants.

Although the genetic code has been in hand since 1966, we have yet to understand its origin. Is the dictionary entirely arbitrary, such that glutamate might equally well have been specified by any other of the 64 possible combinations of the four DNA bases? Or does the particular code that nearly all cells use have some significance: like the etymological entries in a dictionary, do meanings somehow reflect the history of genetic coding?

In her thesis work, Noel Goddard boldly attacked this complex problem. She hypothesized that the genetic code *does* have a nonrandom significance, and specifically that the code is meant to minimize the impact of errors. In a cell, as in any other system that transmits information, mistakes happen. The GAG that specifies glutamate might, for example, be misread as GAC; this would lead to the use of another amino acid, in this instance aspartate. What would be the consequence? Interestingly enough, of all the other 19 amino acids, the one that most resembles glutamate is, in fact, aspartate. So if an error were to be made, this would be the most tolerable error — the change that would wreak the least havoc in the protein finally produced.

Noel endeavored to ask whether such an arrangement is coincidental, or whether the code is so contrived that most errors would be gracefully accommodated. She constructed various strains of bacteria in which she could artificially raise the error rate, then planned to see which errors were judged most egregious by the implacable standard of biology — cell death. Before getting to this experiment, though, she encountered an unexpected difficulty that has proven an unexpected opportunity. When control cells were made that were meant to use the correct amino acid, though too much of it, these cells were found to be just as sick as those designed to be error-prone. What Noel has discovered implies that the amount of each amino acid ready for incorporation into proteins must be very carefully specified. It seems that, if there is too much of some particular amino acid at hand, that substance is likely to be incorporated helter-skelter into numerous inappropriate places, with a ruinous effect on the cell.

Although she has clearly made an interesting and important discovery along the way, Noel has not been deflected from her central interest in the genetic code. Now serving as a junior fellow at Harvard — a by-no-means-unprestigious position at a far-from-negligible institution — she is pursuing the problem of the genetic code with new colleagues, but with her customary vigor and rigor. Her friends and colleagues here at Rockefeller wish her every success in this and her subsequent undertakings.

Mr. President, Mr. Carson, honored guests, it gives me great pleasure to introduce Noel Goddard.

PHOTO: BRUCE GILBERT

A trumpeter announces the beginning of the procession.

Marsha Nidanie Henderson

B.S., Spelman College
Allosteric Features in Src and Abl Tyrosine Kinase Regulation
presented by John Kuriyan

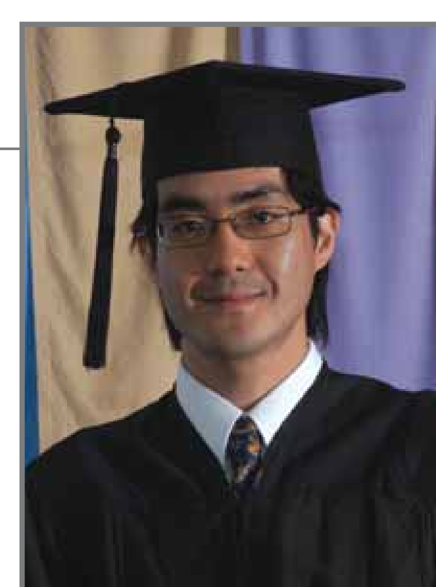
Marsha Henderson came to The Rockefeller University after undergraduate studies at Spelman College and a stint at the biotechnology company Amgen. After working in two other laboratories on a remarkably diverse range of projects, Marsha joined my research group, and began working on the molecular mechanism of action of the drug Gleevec, effective against chronic myelogenous leukemia. Structural studies in my laboratory had shown previously that the specificity of this drug for its target, the protein kinase encoded by the c-Abl and BCR-Abl genes, depends in part upon the recognition of a distorted and inactive conformation of the kinase domain of Abl. Marsha's graduate research has focused on an analysis of how mutations in Src and in the Abl tyrosine kinases affect the ability of these proteins to be activated and to bind to the drug. Since an unfortunate consequence of Gleevec treatment in many patients is the development of mutations that render the protein resistant to the drug, Marsha's work is helping in the important task of understanding the mechanisms of resistance and in coming up with strategies for improving the efficacy of alternative inhibitors of the Abl kinase.

In addition to her strengths as a research scientist, Marsha is also an excellent teacher. Since moving with my laboratory to the University of California, Berkeley, Marsha has taken on the responsibility of selecting and recruiting undergraduate students to our laboratory, and then helping these students find the research projects that would help them realize their potential as research scientists. Marsha's oversight has been responsible for maintaining an extraordinarily high quality of undergraduate engagement in my laboratory, something that is not always easy to accomplish at a large university like Berkeley, where many undergraduates seek out research groups not because they are interested in research but because they feel that this is an important thing to put on their resume. As "dean of undergraduate studies" in the lab, Marsha has ensured that our undergraduate research presentations are one of the highlights of our internal research seminars, and she and I have had the privilege of seeing some these students go on to win awards in campus-wide research competitions. There is no doubt that Marsha will go on to have an impact in the recruitment of students to science wherever it is that she ends up teaching and doing research.

It has been a privilege to have had such a fine scientist and educator as my graduate student at The Rockefeller University.

Mr. President, Mr. Carson and honored guests, it is my pleasure to present to you Marsha Henderson.

Makoto Ishii



B.S.E., Princeton University
Losing GPR7, the Neuropeptide W1 Receptor: Would it Make You Obese, Lazy, Sleepy or Depressed?
presented by Jeffrey M. Friedman

Contrary to what many people think, biologic science requires much more than intellectual acuity and creativity. The successful biologist also needs to have intuition, an ability to assimilate new information, technical and manual skill, social awareness and the ability to work with others, frequently as part of a team, and perhaps most important of all, passion. Few people have all of these traits. Makoto Ishii does.

Mak joined my laboratory in 1999 as an M.D.-Ph.D. student with a spectacular undergraduate record at Princeton. As an undergraduate working in Dallas at the University of Texas Southwestern, Makoto played a critical role in identifying orexin, a then new peptide in the brain that regulates sleep. Deficiencies of orexin are responsible for the human sleep disorder known as narcolepsy. Orexin and other peptides like it function as transmitters of sorts, conveying information from one neuron to the next. These transmitters act on other molecules known as receptors. The receptor for orexin is a member of a class known as G protein-coupled receptors, which is a large family that in aggregate represent perhaps the largest set of drug targets for medicines that treat humans today. Makoto extracted much from his experience and developed an intense interest in and appreciation for G protein-coupled receptors.

By chance, at almost the same time we had developed an interest in another G protein-coupled receptor known as GPR7 that we had reason to speculate might play a role in regulating body weight. Our laboratory focuses on the molecular mechanisms that regulate food intake and energy expenditure, or energy balance. This receptor was expressed in the hypothalamus, a region of the brain that regulates most basic bodily functions including food intake. Indeed, the expression of the receptor was altered in obese animals made so by destroying specific regions of the hypothalamus. Based on his interest and his intuition Makoto set out to study this receptor further. He used a number of sophisticated methods in genetics and neuroscience to establish that indeed this receptor does function in an important way in the neural circuit that controls appetite and body weight. He also established for reasons that we do not completely understand that it does so to a much greater extent in males than females. He also found that it functions independently of leptin, the fat cell hormone that our laboratory identified a decade ago. This work has identified an important new element of the neural circuit that controls appetite and would be extremely important for that reason alone. However because G protein-coupled receptors are such good drug candidates, his work has stimulated enormous interest from the pharmaceutical industry, and almost every pharmaceutical company in the world has licensed the genetically altered mice that he made which lack this important receptor.

This work is attributable to all of the wonderful qualities that Mak exhibits. In addition, he is a warm and generous colleague and is extremely well liked and respected by our laboratory. He has spent the last year in Japan, where he has continued to explore his interest in neuropeptides. He now plans to complete his medical studies en route to what I am confident will be a highly distinguished career in medical science.

Mr. President, Mr. Carson and honored guests, it is my privilege to present to you Makoto Ishii.

Saul Kivimäe

B.S., University of Tartu
Studies on Protein Phosphorylation in the Circadian Clock of Drosophila melanogaster
presented by Michael W. Young

Saul Kivimäe grew up in Estonia. Immediately following secondary school, he attended the College of Natural Sciences where his early inspiration to take on the life of a scientist came from his many tutors (in both the physical and biological sciences) from the ranks of the Estonian Academy of Sciences. After two years at the college he stepped up to more advanced studies at Tartu University. This was a four year program in which he specialized in molecular biology and genetics. His first exposure to the U.S. came through The Cold Spring Harbor Laboratory Summer Undergraduate Research Program, where in 1996 he worked with Dr. Arne Stenlund on DNA replication in papillomavirus. In his application to RU he later described his experience at Cold Spring Harbor as an awakening to the mechanics of science — how knowledge in the sciences is really generated through long hours of benchwork and constant discussion as a laboratory project unfolds.

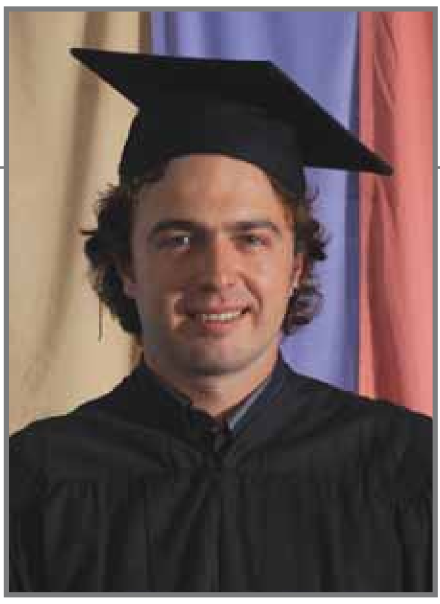
Saul came to Rockefeller's graduate school in 1998, and took my course in genetics in the fall of that year. Saul was especially attracted to ways in which genetics might be applied to very complex biological problems — especially behavior. This was a long way from his training in virology, but he came by the lab wanting to work on a project related to sleep/wake rhythms in our favorite organism, the fruitfly, *Drosophila*. Saul wanted to work on a gene that controlled the stability of a key timing protein in the cell called PERIOD. He wanted to demonstrate that his gene directly controlled a modification, phosphorylation, of the PERIOD protein that determined its duration in the cell. Saul was not the first student to take on this problem, two others had briefly worked on the project and failed, but he was unshaken. After some very careful biochemistry, Saul purified the protein made by his gene and proved that it acted on PER as he suspected.

He also proved the importance of these modifications by making a new series of *period* mutations that specifically blocked the changes made by his protein and dramatically changed the timing of the sleep/wake cycle. Recently a defect in the human version of Saul's gene was found to be the culprit in a familial sleep disorder in humans. Like Saul's mutant flies, humans afflicted with the disorder have sleep timers that run much too fast. Working on this problem also had some totally unexpected benefits for Saul. He met a young woman with similar interests at a scientific meeting a few years ago. Krista was also a graduate student, but less conveniently studying biological clocks in Houston, Texas. We all watched Saul brush aside issues of distance as he first became a commuter husband and then father of Rebekka, a new baby girl. The family is now reunited in San Francisco, where Saul will be pursuing postdoctoral studies in mammalian brain development with Ben Cheyette at UCSF.

Mr. President, Mr. Carson and honored guests, it's my pleasure to present to you Saul Kivimäe.

Pablo Meyer Rojas

Licenciatura, National Autonomous University of Mexico
D.E.A., Maîtrise, Université Paris VII
A New Way of Ticking for the Circadian Clock, FRET Analysis of PER/TIM Interactions
presented by Michael W. Young



Pablo Meyer was born in Perpignan, France. His parents were professors who each held two university positions, one in France and the other in Mexico. Each year of Pablo's childhood was divided according to his parent's transatlantic teaching obligations. In 1994 he entered the College of St. Louis in Paris, where he received a citation in mathematics. True to his upbringing he next enrolled in the National Autonomous University of Mexico, where he majored in physics, graduating in 1997. He then earned, sequentially, two advanced degrees: a Magistere of Physics and a diploma for advanced studies in physics and biology, both from the University of Paris. In 1998 this citizen of the world turned up at Rockefeller to take on biology.

Pablo developed a special interest in biological clocks and came to me wondering whether someone with his background could explore the use of some new biophysical tools in the lab. Pablo particularly wanted to know more about the physical interactions among proteins in a cell that make 24 hour (or circadian) clocks tick. It is known that a cell generates a timer, in part, by controlling where two key "clock" proteins, PERIOD and TIMELESS, reside. The proteins are formed in the cytoplasm during the day and early evening, but are moved to the nucleus late at night where they block their own synthesis. Once PERIOD and TIMELESS move to the nucleus, they are modified and become fragile, so that after a few hours their depletion allows a renewed production of the cytoplasmic proteins. This system oscillates because the cell has developed methods for delaying movement of PERIOD and TIMELESS from the cytoplasm to the nucleus.

This control is what Pablo wanted to understand at a refined level. It was known that access to the nucleus required PERIOD and TIMELESS to find each other and to form a physical partnership. It was believed that the delay needed to build an oscillator came simply from the slow process of finding partners, and that partnership was the complete ticket to the nucleus.

Pablo followed the process by engineering new forms of the PERIOD and TIMELESS proteins that would fluoresce when in physical contact in the cell. He followed the journey the proteins made to the nucleus in real time using a special microscope, as well as the timing of their partnering. Pablo surprised us all when he found that PERIOD and TIMELESS partnerships were formed within minutes, but these assemblies nevertheless remained in the cytoplasm for about five hours. At that point the proteins abruptly separated and independently moved to the nucleus. In the fruitfly there is a mutation of PERIOD that causes the sleep/wake cycle to occur with a 29- rather than a 24-hour period. When Pablo followed this mutant PERIOD protein in his cells he found that again assemblies formed immediately, but broke apart and entered the nucleus after nine rather than five hours. Pablo discovered that somehow, when brought together, PERIOD and TIMELESS form an interval timer that begins to wind down at a rate that can be very precise and specified by the proteins themselves.

Pablo will be going on to new postdoctoral work at Columbia in the fall. He will be studying protein assemblies with these and new tools that control differentiation in a sporulating bacterium.

Mr. President, Mr. Carson and honored guests, it's my honor to present to you Pablo Meyer.

PHOTO: BRUCE GILBERT

Bob Darnell hugs his student Jernej Ule following his speech in Caspary Hall.

PHOTO: BRUCE GILBERT

Robert Schoenfeld, Norton Zinder, Brian Chait, Emil Gotschlich and Tom Muir march in the Convocation procession.

Ernesto J. Muñoz Elías

B.A., Rutgers University
Targeting Mycobacterium tuberculosis *Metabolism during Infection*
Presented by John McKinney

Ernesto Muñoz came to us here at Rockefeller from Rutgers University and he joined my lab when I was still a newly minted assistant professor, and in a nutshell, Ernesto's the kind of student that every new assistant professor dreams and hopes they'll get, and usually they don't get that lucky, but I did get that lucky. He's really a truly exceptional individual I think even by Rockefeller standards. And when I say exceptional I don't mean that he's brilliant and talented and has golden hands and has a passion for his research and hunger for knowledge. Of course all that's true, but that's true of all of our students and we expect that of our students.

There are two things, however, that I think really stand out about Ernesto and make him quite special. The first is his really extraordinary tenacity. You know, as was mentioned I think by Tshaka today, we all experience a lot of failures and setbacks in our work. That's normal. It's inevitable. We expect it. But in a slow field like TB, which is inherently slow because of the behavior of the organism and where a single experiment can often take upwards of a year to complete, the usual setbacks can be really quite devastating for a young investigator. Ernesto certainly had his share of setbacks, as we all do, but he never got discouraged. It was astonishing to watch. He never gave up and he never stopped pushing. And I think really without exception his response to every roadblock that he met was a very a simple one: worker harder, push harder.

I would say, in sum, that he displays qualities of persistence and resilience that really rival the organism, the *tubercle bacillus* that he studied. In fact, it was the problem of persistence in tuberculosis that he focused on because he believed, as I do, that this is the key to understanding the pathogenesis of this disease and the key to unlocking better therapies of treatment of tuberculosis. So what I'm trying to say is that what this quality that Ernesto possesses really in spades, which I can only refer to as guts, is probably, in my opinion, the single, most reliable predictor of success in science. And I am quite confident that we can expect to see great things out of Ernesto in the future. So that's the first thing that I think is really quite extraordinary about Ernesto.

The second thing is that he truly is a social idealist and I don't mean that in the armchair sense of the term. He really lives his ideals, which is quite unusual. And he brings the same kind of passion and dedication to this arena that he brings to his research. In fact the two are not separate in his mind. I think this is one of the many way in which we are like-minded. In fact, the reason why he chose to study a problem like tuberculosis, which is a disease that is historically, and still today, very intimately linked with poverty, is that he has very deep concerns about the enormous and ever-growing inequalities and inequities in the global human condition. I'd just like to point out that we live now in a world where the wealthy have become fabulously wealthy and we've left a lot of the world behind. We live in a world where those of us who frankly have just the sheer dumb luck, that's all it is, to be born in a wealthy country like the United States, can expect to get another 40 years or more of life than those who live in the poorest country who represent, actually, a much larger number of people on the global scale.

I feel that this has got to change. Ernesto also feels that this has got to change and this is the century in which we have to accomplish this. And he shares my conviction that science is going to be one of the keys to this change and there are exciting things happening in the world now. What's remarkable about Ernesto is that he already knew this at the time and felt it very deeply when he matriculated at Rockefeller University. He had that level of maturity. This is something that took me many many years of reflection to arrive at. And it's the conviction that science, when it's properly focused, can be a very powerful engine for social justice and I think that's a lesson that perhaps we could do a better job than we currently do of teaching our students.

I'd just like to mention parenthetically that he's already had a taste of that. His work, which is focused on understanding metabolic pathways that are involved in persistence of *M. tuberculosis* in the human body, has formed the basis for drug discovery programs now that have been sparked at several pharmaceutical companies and last month, the Global Alliance for Tuberculosis Drug Development, which is a non-governmental organization, a splinter, if you like, of the Gates Foundation, focused on TB drug development, announced a strategic partnership with one of those companies, Glaxo Smith Kline, to develop new drugs for treatment of tuberculosis. And I just wanted to point out that the foundation of that strategic partnership is Ernesto's work in my laboratory.

So, in sum, I really can't tell you how proud I am of this young man. And I have mixed feelings about standing up here today because although I am immensely proud of him and I look forward to seeing the great things he is going to do in the future, his departure from the lab is going to be a real loss, both professionally and personally. I'm proud of his accomplishments. I'm proud of his ideals. I'm proud of the way he lives his ideals through his work, everyday he spends in the lab. He's been really a superb colleague, a dream colleague, and he's been a very good friend as well.

So Mr. President, Mr. Carson, and honored guests, it's my pleasure and my very great privilege to present to you Dr. Ernesto Muñoz.

Mario Niepel

Diplom, University of Aachen
M.S., University of California at Riverside
The Myosin-like Proteins in S. cerevisiae*: Multifunctional, Structural Components of the Nuclear Envelope*
Presented by Michael P. Rout

It's my very great pleasure to introduce Mario Niepel for the degree of doctor of philosophy. Upon joining my lab, Mario decided to tackle a formidable challenge — namely, to try to understand more about the nuclear envelope, which is the protective barrier surrounding the nucleus and the DNA in our cells. Scattered across the envelope are many small circular channels, called nuclear pore complexes, which acts as the gatekeepers of the nucleus. By regulating what can get in and out of the nucleus, the nuclear envelope can play a crucial role in controlling which of the instructions in the DNA are active. Moreover, the nuclear envelope is key to controlling how the DNA, and so cells, divide at mitosis.

Together with Caterina Strambio-de-Castillia, Mario focused on a pair of proteins that project out of nuclear pore complexes into the nucleus. Using baker's yeast as a model organism, they showed that these proteins form a network, connecting up between the nuclear pore complexes around the periphery of the nucleus, and perhaps forming a platform for the proper assembly of RNA messages as they leave the nucleus. Most strikingly, they showed that one of these two proteins also attaches to the spindle organizer. In doing so, it plays an important role in helping the cell divide properly.

During his time in the laboratory, it became clear that Mario has a blend of talents that will undoubtedly prepare him for a tremendous future in science. He is intelligent, thoughtful, and an excellent experimentalist. Moreover, he showed an incredible determination, in the face of tremendous difficulties in his project. Because of his dedication, he overcame these obstacles and his project has grown into a major piece of work. It has also led to new lines of research that even now are still bearing fruit.

Mario has also proved to be a great colleague to others in the laboratory, happy to offer a helping hand or advice. Indeed everyone in our laboratory would enthusiastically agree that Mario is a fantastic team player who has contributed tremendously both to the scientific and social life of the laboratory. In fact he combines his scientific and social skills in his talents as an excellent cook. If the way to someone's heart is through their stomach, then Mario has definitely conquered us all with his numerous tasty dishes — and if there were any doubters, they would be rendered insensible by his high octane Gluwein.

After a brief period finishing up work in my laboratory, Mario will be continuing his career as a postdoc in Boston where he will without question flourish. We will all miss him but of course we wish him all the best.

Mr. President, Mr. Carson and honored guests, it is my pleasure to present to you Mario Niepel.

Vanessa J. Ruta

B.A., Hunter College, City University of New York
The Structural and Functional Analysis of a Voltage-dependent Potassium Channel
presented by Roderick MacKinnon

On September 29, 1999, I received an e-mail from a young Hunter College undergraduate: "Dear Dr. MacKinnon, I met you this summer when you gave the Friday evening lecture at MBL…" She went on to write: "To me, you seemed to embody the unbridled enthusiasm of scientific curiosity which I find so appealing and hope to share." Knowingly or not, Vanessa described herself with great accuracy selecting those words "unbridled enthusiasm of scientific curiosity."

Vanessa was to graduate from Hunter early, in January, and was eager to start her life as a graduate student, or, in her words "to delve into one scientific question without limitations." Vanessa's second email to me read: "I have given serious consideration to your suggestion that I might wait until September to begin in the lab but I think I would prefer nevertheless to go ahead and join you…" This began an incredible journey for me and, I think, for her.

Voltage-dependent ion channels are unusually stubborn beasts of molecules that refuse to yield to the conventional weapons of the protein crystallographer. But they are important. They make the electrical impulses that travel rapidly from your brain to your muscles when you move and from one nerve cell to the next when you think. What do these ion channels look like and how do they work? These are the questions that Vanessa and a small group of other very talented scientists have tried to answer in my laboratory.

Vanessa captured a picture of one of these voltage-dependent ion channels in a most clever use of the X-ray beam, Fourier transforms and crystal symmetry. And she measured its surprisingly large movements using a truly unconventional weapon — so unconventional that most other scientists in the field are still trying to comprehend the meaning of your results. This is a good thing. Unconventional is good. I am certain that Vanessa's experimental results will be described in textbooks once people have had some time to ponder their significance. Through her unbridled enthusiasm of scientific curiosity she has made a very big difference to our understanding of voltage-dependent ion channels.

Vanessa is an intense, passionate, gifted scientist. In fact, I have never had a student in my lab at Harvard or at Rockefeller at Vanessa's level. Her passion comes not from wanting to understand how to fix a certain problem or cure a certain disease, it comes from a deep, deep curiosity and wanting to understand the inner workings of nature. Vanessa has accomplished three times what she needed to get her Ph.D., and this was out of her own internal drive and curiosity. She was the recipient of the David Rockefeller Fellowship award as a third-year graduate student, and this year she won a Harold Weintraub national award that is given to a small number of the top graduate students in the United States in biomedical science. Vanessa has been to me an outstanding student, colleague, and a true friend. She'll be going to Columbia University where she'll undertake her postdoctoral studies with Richard Axel and it won't take Richard very long to realize how lucky he is.

Mr. President, Mr. Carson and honored guests, it is my pleasure to present to you Vanessa Ruta.

Sukhvinder Sahota

B.A., Rutgers University
The Seven Month Itch … The Role of an E3 Ligase in Immune Response Modulation
presented by Alexander Tarakhovsky

Sukhvinder Sahota graduated Rutgers University and remained a true patriot of the state where she graduated. I remember riding a bus with her when we went to a meeting in Tuscany, and she looked out the window and said, "Great, that looks exactly like New Jersey." And if I ever had a chance to write a book about scientific life, in a part related to Sukhvinder I would say my personality got split one day and I felt like Fernando Nottebohm. And the reason for that is that Sukhvinder truly is not talking, she is chirping. And the singing with different sounds is very inspiring as a melody but also has a very true meaning. You don't need to talk to her. You just need to listen to the sound to understand whether the experiment was working okay or not and whether it's fine for me to approach her or should I better lock myself in the office.

So I will greatly miss Sukhvinder. I'm actually missing her and I don't know whether it's appropriate to say, but I feel like I lost her to medical science. But of course I can also see that medical science gained an outstanding person who, during her relatively short stay in my lab, contributed to a great extent to our understanding of the mechanism of autoimmunity. She studied a single protein, an ubiquitin ligase, that many of you know is involved in regulation of protein stability, and found that this one protein is an essential component of a signaling network operating specifically in T-lymphocytes that single-handedly can control diseases in mice that look very similar to diseases in humans, like psoriasis or general inflammation and so on and so forth.

It is an absolute honor for me to be Sukhvinder's mentor. I'll greatly miss her and I hope that all people who know her here will share the same feelings with me.

So Mr. Carson, Mr. President, it's a great pleasure to introduce Sukhvinder Sahota.

Bahar Taneri

B.A., Ohio Wesleyan University
Comparative Analysis of Alternative Splicing in Human, Mouse and Rat Transcriptomes
presented by Theresa Gaasterland

It's a joy to present to you today my student who's actually the fourth student in three years to graduate from the Computational Genomics Laboratory, my laboratory here at Rockefeller. Bahar came here from Ohio Wesleyan, but where she really came from was this island off the coast of Greece, called Cyprus, but she is from Turkish Cyprus. And that was always her test to anybody who came into the lab: Did they know that there was this little part of the island with this little population? And as she recognized that people were politically savvy or not, she would educate them. And this was actually a property that she brought to her science. Whenever somebody would come into the lab with a bioinformatics question wondering, "How do I search this sequence? How do I use this tool? How do I turn on the computer?" Bahar was always very patient and she showed them where the switch was, and she got them started.

So three years ago, she came into my lab from Hermann Steller's lab, wondering, "I'm tired of asking questions about just one gene. We've got this human genome now; I should be able to ask a question that involves lots and lots of genes. Terry, do you have a good question for me to ask?" And I said, "Yes, but it means you have to program." And she said, "No problem, I'll learn how to program."

So she went trotting off, taught herself how to program, came back and started working on the entire human genome all at once, looking for transcription factors that were alternatively spliced. And she focused in to ask the question, not how is alternative splicing controlled, which is what everybody was asking, she said, "Eh, let's set that aside and ask: why does it matter? What are these alternatively spliced transcription factors doing? Can we enumerate all of them? Can we figure out what every one of them is doing?" And relentlessly, for three years, she pursued this question.

Along the way she ran into Jernej Ule in Bob Darnell's lab, who was asking the question: We've got this alternative spliced protein Nova that controls alternative splicing. We don't really know all the things it does. So, Jernej and Bahar teamed up and formed a very tight bond between my lab and Bob Darnell's lab where we'd been trying to pursue what exactly is going on with all this alternative splicing that's running around in the human genome.

So, very very recently as Bahar was finishing her Ph.D., she started asking the question: well, what's the difference between pathological alternative splicing, accidental alternative splicing, and biologically significant alternative splicing? So she focused on cancer and tried to characterize the alternative splice forms specific to cancer cells, things that are entirely pathological. And then she turned to a harder question which was: there are proteins in tissues like the brain that suddenly get expressed in tissues like the lung when those cells become cancer cells. And this has a profound impact on whether the body is going to respond and attack that cancer. So she decided to turn that into computational questions and start cataloging tissue specific proteins misexpressed in certain other tissues that had become cancer cells.

So as Bahar finishes, she's going back and she's going to try and educate people back in Turkish Cyprus. And she's going to continue to educate me. She's going to work with me doing a postdoc for the next six months, at least; the next 10 years if I can keep her. And she'll be working on these cancer-related questions and hopefully opening new horizons.

So Bahar, I hope you always keep asking, "What does this mean? What is going on in this genome and why is it important?" and using "Why is it important?" to focus your investigation as you always have and then grounding that in "How does that work?"

So Mr. President, Mr. Carson, and honored guests, it is my pleasure to present to you Bahar Taneri.

Jernej Ule

B.S., University of Ljubljana
Nova Regulates Brain-specific Splicing of RNAs Encoding Synaptic Protein Networks
presented by Robert B. Darnell

Having graduate students in the lab is a bit like having children in the family — they are all equally special. Yet living with Jernej Ule over the past three years, I cannot help but have the feeling that in some ways, to turn an Orwellian phrase, he is just a bit more equal.

Jernej seemed to come to the lab from a lost time and place, a renaissance scholar emerging from the mist into the big city. He was born, raised and educated in Ljubljana, Slovenia. In this tiny spot, his grandparents, farmers, produced two university professors, who in turn cultivated Jernej's intellectual curiosity and sweet, almost naïve honesty, both of which I've seen shine through at RU.

Before coming here, he was an undergraduate at the University of Ljubljana, where he was an outstanding student, a 9.23 GPA, winning first prize in a mathematics competition, the Krka award for the best undergraduate research project (on HIV), and performing as a concert pianist. He was accepted to the University of Cambridge and to Rockefeller University for graduate studies, wisely choosing the latter. He immediately sent a request to come early and start working, along with a telling letter to the housing office requesting a bigger apartment, explaining "…I met her three years ago in Italy … this year she (Betina) came to New York; we met soon afterwards and fell in love." Once here, he started off running and never looked back. In his first rotation in the Greengard lab he published two papers. He joined our lab in September 2001 and began working with a postdoctoral fellow, Kirk Jensen, on an old project that had been put on the backshelf. He soon stunned the postdoc by turning the project into the premier work in the lab. Resurrecting a difficult set of experiments and techniques, Jernej worked assiduously to develop a new and groundbreaking way of identifying the exact sites that regulatory proteins bind to genetic material inside living tissues, a technique we termed CLIP. This work was of special importance because such interactions provide a key to understanding a number of important brain diseases such as the Fragile X mental retardation, and we now suspect they are likely to be more generally relevant in diseases like cancer. His work was widely recognized in an important paper published in *Science* magazine. But Jernej did not rest there, instead repeating his effort with a second backshelf project, putting together his mathematical skills (together with his brother, a mathematician working on his Ph.D. in Amsterdam), biochemistry, and focus, to develop sterling data from a new DNA chip being developed by the company Affymetrix. This work, now in press in *Nature Genetics*, together with Jernej's first study, has established a new way of thinking about a complicated and unexpected network by which the information present in our genes is used in our brains.

Through all this, Jernej has been able to make friends and colleagues all across the university and the world of science, to nurture his own small family, and to find time to be on call as a page turner for pianists at the Friday concert series. In short, Jernej has risen to the very top of the talented group of students I've been fortunate to have: equally wonderful to work with, to think with, and to be proud of. We look forward to great things from you, Jernej, and wish you the best of luck.

Mr. President, Mr. Carson, and honored guests, it is my pleasure to present to you Jernej Ule.

PHOTO: BRUCE GILBERT

Mike Young, John McKinney, Rod MacKinnon, Terry Gaasterland and Titia de Lange, all faculty presenters, during the ceremony in Caspary.

Jernej Ule's daughter, Ladja, tries on her father's cap.

Richard C. Wang

B.S., Stanford University
Homologous Recombination and Chromosome Ends: TRF2 Keeps Telomeres Out of the Loop
presented by Titia de Lange

Richard Wang came to our Tri-institutional M.D.-Ph.D. program from Houston via Stanford. He decided to join my lab in the summer of 2000 and defended his thesis four years and three months later. I stress that Rich joined my lab based on his decision, not mine. I felt that I already had too many students in my lab but Rich simply did not take no for an answer. He wore me out with e-mailed suggestions for projects and new techniques and I said yes in the end. This persistence is typical of his approach to everything he cares about, in the lab and outside.

Rich's tenacity became an important factor in his success, as was his ability to ignore my opinion. Easily excited about seemingly impossible projects, Rich took on the most difficult problem then available in my lab: the enigmatic phenotype of a mutant version of the telomeric protein TRF2. His careful analysis of this mutant uncovered a new pathway that threatens human telomeres. Rich discovered that large chunks of telomeric DNA can be deleted suddenly through homologous recombination, a finding with ramifications for the growth and aging of human cells.

Rich argued that this pathway cuts off the telomeric t-loop and he wanted to demonstrate this by looking for circular telomeric DNA on 2D gels. I remember very clearly how I explicitly and emphatically counseled against this approach, which I deemed too difficult, even for Rich.

True to character, Rich ignored me and did the experiments without telling me. The cover of the November issue of *Cell* last year showed how wrong I was. It features Rich's 2D experiments in all their glory, a permanent witness to everything Rich stands for: tenacity combined with creative thinking and unmatched experimentation skills.

Rich's energy is astonishing and so is his craving for knowledge. All kinds of knowledge. He is an information junky who binge-reads and wants to know the details of everything. He also wants to do everything, including every possible experiment you can think off. Arguably, my main contribution to Rich's Ph.D. was to keep him focused on just two projects rather than 10.

Now back in the clinic, Rich will finish his medical training before returning to basic research. I expect him to make a major impact on biomedical sciences once he is back at the bench. In the meantime, he will continue to be a great friend to the lab and a wonderful caring son and brother.

Mr. President, Mr. Carson and honored guests, it is my pleasure to present to you Richard Wang.

Pauline Yoong

B.Sc., B.A., University of New South Wales
A Novel Approach in the Control of Antibiotic Resistant Enterococci and the Bioteror Agent Bacillus anthracis
presented by Vincent A. Fischetti

Bacteriophage, or phage for short, are viruses that infect bacteria. After entering a bacteria and producing a hundred or more progeny phage, they have a problem: they need to get out of the infected bacteria to start a new cycle. They solve this problem by producing an enzyme that will digest the bacterial cell wall allowing the bacteria to explode. These are very potent enzymes. For example, a small amount of purified enzyme added to a hundred million bacteria will reduce them to 10 in a matter of seconds.

Pauline Yoong cloned the gene for two different phage-lytic enzymes: one that was specific for the *Enterococus*, the organism that is responsible for serious disease in hospitals, and anthrax, the bioterror agent. Pauline then purified these two different enzymes and showed that they can kill their respective organisms rapidly and on contact. She also showed that the enzyme could quickly kill newly germinating spores.

This method of decontaminating spores could prove to be very useful. For example, if there were an intentional spill of about a pound of anthrax spores in New York City, using current methods, it is estimated that it would take 42 years to clear out the spores so the area could be reinhabited. So Pauline's enzyme could be combined with other current methods to shorten the process. The *enterococcal* enzyme, on the other hand, could be used in hospital setting to safely remove *enterococci* from the environment and the mucus membranes of hospital patients and staff to reduce the source of infection.

On a personal note, you wouldn't know it by looking at her, but Pauline has a dessert fetish. She is personally working her way through all the bakeries in New York City, tasting the various specialties of that bakery. Of course, only Pauline would do this very scientifically by following the recommendations of the *Zagat Survey for New York Bakeries*. I believe to date she is about 25 percent through the list and is still as petite as ever.

Pauline will stay on in the lab to continue her exciting enzyme studies but is considering a position in Harvard.

President Nurse, Mr. Carson, it is my pleasure to present Pauline Yoong for doctor of philosophy.

The next generation…

Nearly 700 aspiring scientists applied to take the spots vacated by this year's graduating class, a record applicant pool for the university's graduate program. This winter, the Dean's office — along with a committee of eight faculty members — vetted applications. In February, 10 percent of the applicants were accepted and 22 enrolled.

The new class, 12 women and 10 men, includes representatives of Argentina, Bolivia, Canada, England, France, Germany and Japan, as well as the United States. They come from 21 undergraduate schools: Arizona State University, Brandeis, Carleton, Duke, The California Institute of Technology, Harvard, Lycee Carnot-Dijon, Mount Holyoke, Portland State University, Okayama University Medical School, Oxford, SUNY Stony Brook, the University of Buenos Aires, the University of California Santa Barbara, the University of Kansas, the University of Pennsylvania, the University of Technology Berlin, the University of Toronto, the University of Tokyo, the University of Virginia, and Wellesley College. They range in age from 20 to 26.

"In addition to great academic records, the admissions committee looks for students with a spark, something that distinguishes them," says Assistant Dean Emily Harms. "Students who tend to thrive at an unconventional university like Rockefeller are independent, creative and fearless. We are incredibly pleased with our incoming class."