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The Rockefeller University

SCIENCE FOR THE BENEFIT OF HUMANITY

BENCHMARKS

THE COMMUNITY NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

FRIDAY, JULY 3, 2009

2009 is a landmark year for science. The 200th anniversary of the birth of Charles Darwin, father of evolutionary biology, and the 150th anniversary of the publication of his classic text On the Origin of Species, *this year is being marked with tributes across the world. It is also a milestone year for The Rockefeller University, which on June 11 celebrated the largest graduating class in its history.*

The 41 graduates of the class of 2009, the fifth class of the David Rockefeller Graduate Program, brings the number of scientists with Rockefeller Ph.Ds. to 1,010. This year's graduates include 28 men and 13 women from Albania, Bulgaria, Canada, England, Germany, India, Italy, the Netherlands, New Zealand, the South Pacific island of Niue, Switzerland, Taiwan, Turkey and the United States.

Of the 30 students in the Ph.D. program, 23 will go on to postdoctoral research, one will attend medical school, one will enter law school, one will be a consultant, one will take time to care for her newborn and three are considering their options. The 11 M.D.-Ph.D. students will return to medical school to finish their M.Ds.

This annual Convocation issue of BenchMarks *salutes the Rockefeller University class of 2009.*

CONVOCATION 2009

FOR CONFERRING DEGREES

Thursday, the eleventh of June

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

PHOTOS: HEATHER LASZLO AND ZACH VEILLEUX

BENCHMARKS

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Cech and Greenberg presented with honorary degrees

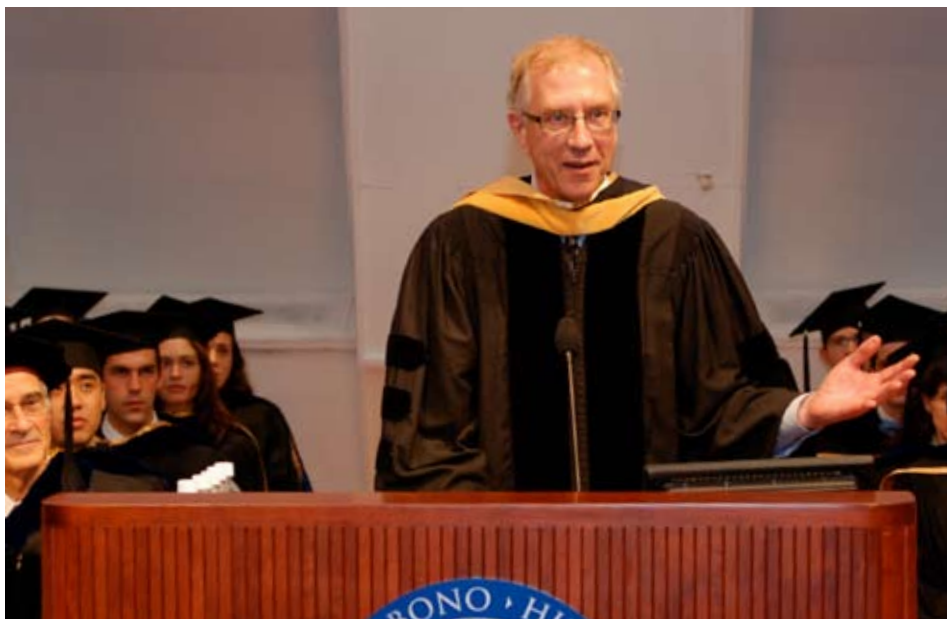
by TALLEY HENNING BROWN

Generations of new scientists have been affected by the work of Thomas R. Cech and Maurice R. Greenberg. Dr. Cech, former president of the Howard Hughes Medical Institute and a dedicated teacher for over 30 years, has long been an advocate for the advancement of young scientists. Mr. Greenberg, chairman of The Starr Foundation and active in numerous other philanthropic initiatives, has made a second career of supporting the most innovative research. The recipients of this year's honorary doctor of science degrees, Dr. Cech and Mr. Greenberg spoke at the June 11 afternoon Convocation ceremony.

A graduate of the University of California, Berkeley, Dr. Cech joined the faculty of the University of Colorado, Boulder, in 1978. Four years later, he made a revolutionary discovery that would overturn long-held assumptions about ribonucleic acid. Demonstrating that a fragment of RNA from the single-celled pond organism *Tetrahymena* could cut and rejoin chemical bonds in the complete absence of proteins, Dr. Cech redefined RNA as more than just a passive carrier of genetic information, and proved that proteins are not the only catalysts. For this finding, Dr. Cech shared the 1989 Nobel Prize in Chemistry. He later went on to study the structure and function of telomeres, repetitive DNA sequences that protect the ends of chromosomes from natural degradation processes. In addition to the Nobel Prize, Dr. Cech is the recipient of a National Medal of Science and an Albert Lasker Basic Medical Research Award and a member of the National Academy of Sciences.

Dr. Cech currently serves as Distinguished Professor in the department of chemistry and biochemistry at CU Boulder, director of the Colorado Initiative in Molecular Biotechnology and an investigator at the Howard Hughes Medical Institute (HHMI). As president of HHMI from 2000 to 2009, Dr. Cech led one of the nation's largest philanthropically funded organizations devoted to biomedical research. During his tenure, he expanded HHMI's reach by opening its first freestanding research facility, introduced focused competitions to identify exceptional physician-scientists engaged in patient-oriented research, broadened the HHMI investigator competitions to embrace more interdisciplinary research and initiated the institute's first ever Early Career Scientist competition.

Referencing Abraham Flexner, brother of Rockefeller's first president and a staunch advocate of progressive educational ideologies, Dr. Cech extolled for the graduates the virtues of including teaching in their career plans. Not only will they make an important contribution to the development of generations of scientists to come, Dr. Cech explained, but teaching will also add a unique source of gratification to their personal lives and will benefit their research. "I have one word of advice for the new Ph.Ds., and that is: Teach," said Dr. Cech.



PHOTOS: HEATHER LASZLO

Honoris causa. Thomas R. Cech, top; Maurice R. Greenberg, bottom center.

At the age of 17, Maurice Greenberg hid his real age and joined the American Army in its World War II campaign, serving in Normandy, France, and participating in the liberation of the concentration camp at Dachau, Germany. Mr. Greenberg also served in the Korean conflict, achieved the rank of captain and received a Bronze Star. In between military tours, he earned a law degree from New York Law School and was admitted to the New York Bar in 1953. Mr. Greenberg joined C.V. Starr & Company as vice president in 1960. He was elected director in 1965, president and CEO in 1968 and chairman and CEO in 2005. In 1962, he took over presidency of the American holdings of American International Group, becoming president and CEO of the company in 1967 and chairman and CEO in 1989. Under his leadership, AIG became the largest insurance company in the world. Mr. Greenberg retired from AIG in 2005.

Mr. Greenberg was elected to The Rockefeller University Board of Trustees in 1997. He is chairman emeritus of New York-Presbyterian Hospital and the New York-Presbyterian Hospital Foundation. He is a member of the board of overseers of Weill Cornell Medical College and chairman of the Academic Medicine Development Company. Mr. Greenberg has served on the boards of New York University, the American Museum of Natural History and the Asia Society, where he was chairman. He is honorary vice chairman and director of the Council on Foreign Relations and an honorary trustee of The Museum of Modern Art and is active in a number of other civic and charitable organizations. As chairman of The Starr Foundation, he oversees the disbursement of significant financial support to academic, medical, cultural and public policy institutions.

Mr. Greenberg has long been a champion of inter-institutional collaboration. In 2000, he launched the Tri-Institutional Center for the Study of Hepatitis C. As head of The Starr Foundation, in 2005 he provided $50 million for the creation of the Tri-Institutional Stem Cell Initiative, in response to the federal funding restrictions placed by George W. Bush's presidential administration on embryonic stem cell research. Speaking before the graduates June 11, Mr. Greenberg said, "The easiest thing to do is be successful in business; the hardest thing to do, I think, is to be a great researcher, and I take my hat off … in honoring their work and their contributions."

Fifth annual teaching awards honor Hudspeth and Nottebohm

by TALLEY HENNING BROWN

While more than 1,000 students have braved the rigors of scientific pursuit to earn Rockefeller University doctorates, the faculty who mentored them have braved some rigors of their own: years of difficult questions, wild experimentation and attentive collaboration. Two of those faculty were honored for their untiring efforts at this year's Convocation Luncheon. A. James Hudspeth, head of the Laboratory of Sensory Neuroscience, and Fernando Nottebohm, head of the Laboratory of Animal Behavior, are the recipients of the 2009 Rockefeller University Distinguished Teaching Awards.

Instituted in 2005 to recognize outstanding individual contributions to the university's educational environment, the teaching award is presented each spring 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. Hudspeth was educated at Harvard University, where he received a bachelor's degree in biochemistry in 1967, an M.D. in 1973 and a Ph.D. in 1974. After postdoctoral work at the Karolinska Institute in Stockholm, he conducted research and taught on the faculties of the California Institute of Technology, the University of California, San Francisco, and the University of Texas Southwestern Medical Center at Dallas, where he founded the school's neuroscience program. Dr. Hudspeth came to Rockefeller in 1995 as the F.M. Kirby Professor and he also serves as director of the university's F.M. Kirby Center for Sensory Neuroscience.

PHOTO: HEATHER LASZLO

Those who can, teach. From left, Fernando Nottebohm, Paul Nurse and A. James Hudspeth at the Convocation Luncheon.

Dr. Hudspeth studies the intricate system that enables hearing in humans and animals. His laboratory has made much progress in understanding sensorineural hearing loss, otherwise known as "nerve deafness." Caused by damage to the hair cells of the inner ear, this type of hearing loss is usually permanent, as hair cells do not self-repair once they are injured. Beginning in 1998, Dr. Hudspeth has teamed with Albert J. Libchaber, head of the Laboratory of Experimental Condensed Matter Physics, in teaching four courses: Impact of Thermal Noise on Biological Processes; Statistical Mechanics: Information Theory and Computation; Materials and Life; and Genetic Information. Last year, when the Dean's Office received numerous requests from students for an introductory neuroscience course, Dr. Hudspeth volunteered. When Fundamentals of Neuroscience was opened for enrollment, the class filled up in two days.

Dr. Nottebohm came to Rockefeller as assistant professor in 1967, the year after completing his Ph.D. at the University of California, Berkeley. He became associate professor in 1971 and professor in 1976 and now serves as the Dorothea L. Leonhardt Professor. He also directs the university's Center for Field Research in Ethology and Ecology, the 1,200-acre plot in Millbrook, New York, where researchers study various organisms in their natural settings.

Dr. Nottebohm's research focuses on the neural mechanisms that underlie a bird's ability to learn its species-specific song. His work in vocal learning resulted in the discovery that certain kinds of neurons in the adult brain can regenerate. Dr. Nottebohm taught his first class at Rockefeller in 1970: Tutorial on Ethological Theory. Since then, he has organized a course in the neurobiology of learning and brain repair every other year. He is also actively engaged in the student recruitment process, leading weekend trips for potential students to the Center for Field Research.

Sarah Wacker named 2009 David Rockefeller Fellow

by TALLEY HENNING BROWN

When it came time to choose a graduate school, Sarah Wacker's method looked a little like a game of darts. Certain that she wanted to continue her study of proteins in a lively urban environment, she applied to what she considered the best school in every major city across the country. "I visited every school I applied to, and when I was accepted to Rockefeller, it felt right," Ms. Wacker says. "Like hitting the bullseye." Having now finished her third year in Tarun Kapoor's Laboratory of Chemistry and Cell Biology, Ms. Wacker's record is still going strong. This spring, she received the university's prestigious David Rockefeller Fellowship.

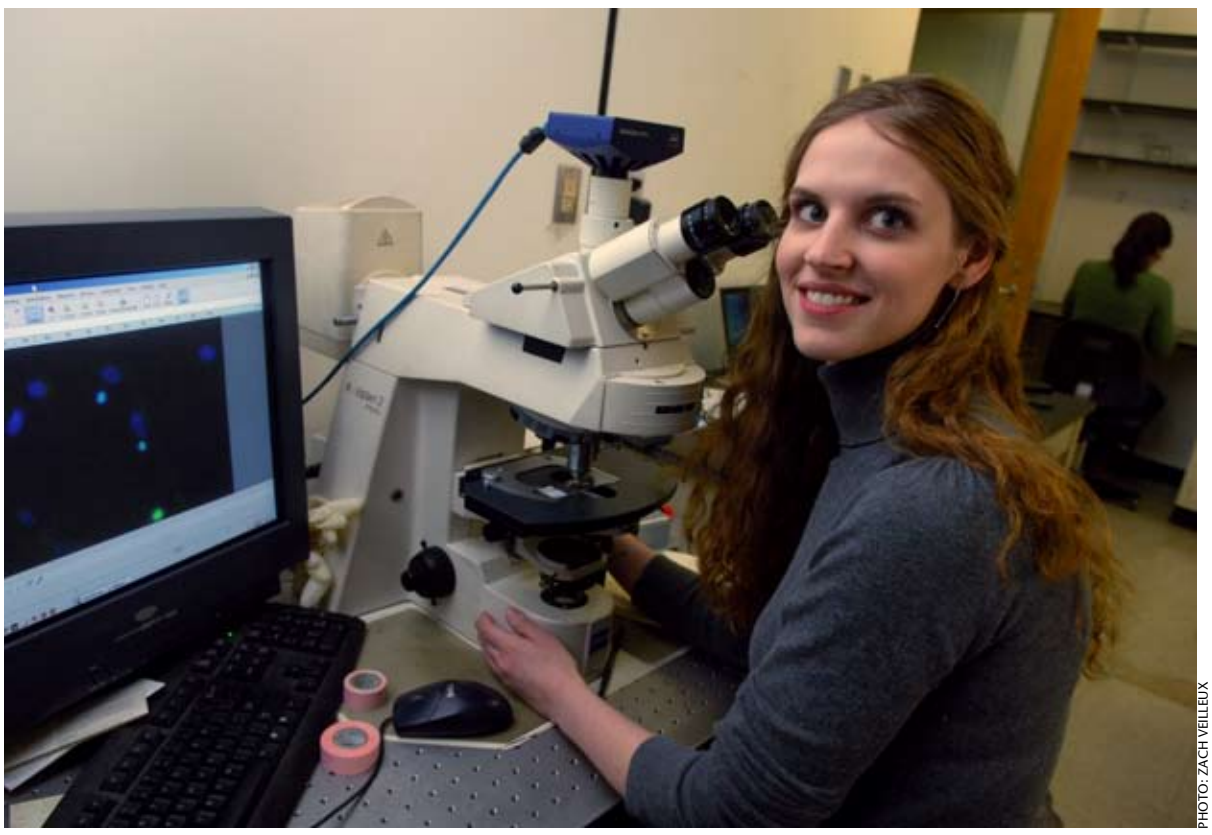


PHOTO: ZACH VEILLEUX

Originally from Perham, Minnesota, Ms. Wacker received her bachelor of science in biochemistry and molecular biology from the University of Richmond in 2006. During her junior year there, she spent a semester studying molecular biology and genetics at Denmark's International Study Program and a summer in the laboratory of Catherine L. Drennan at the Massachusetts Institute of Technology. Along with her research, Ms. Wacker was an active participant in several scientific and volunteer organizations in college, serving as student representative of the National Protein Society Education Committee, vice president of the University of Richmond chapter of the Circle K International Service Organization, president of the Biochemistry Club and newsletter editor of the American Chemical Society Student Affiliates Club.

Now at Rockefeller, Ms. Wacker's research is narrowing in on the mechanisms of the cell cycle. Currently, she is working to develop a novel approach to generate small-molecule inhibitors for a family of motor proteins known as kinesins. Because kinesins are intimately involved in the processes of mitosis and meiosis, their inhibition might have implications for cancer research, but Ms. Wacker is mainly interested in what they can reveal about cell division. "Kinesins have myriad functions in the cell," says Ms. Wacker, who has received numerous accolades during her few years in research, including graduate fellowships from the National Science Foundation and Rockefeller's *Women & Science* initiative, as well as the university's inaugural George Palade Fellowship, awarded to her in March.

Since her first year at Rockefeller, Ms. Wacker has also maintained a busy volunteer schedule. In the spring of 2007, she was a mentor with the Cornell Science Challenge, a Tri-Institutional community-education program in which mentors from Rockefeller, Weill Cornell Graduate School of Medical Sciences and Memorial Sloan-Kettering Cancer Center guide groups of seventh-grade students from East Side Middle School in developing original research projects. She has served as a journal club adviser for Rockefeller's Summer Undergraduate Research Fellowship program and has worked on the selection committee for the Summer High School Science Outreach Program. And she has volunteered as a judge for the New York City Science and Engineering Fair every spring since moving to New York. "My ultimate goal is to teach science, preferably at the undergraduate level," says Ms. Wacker. "My experiences both as a mentor to younger students and as a student here, where you can't help but learn so much from everyone around you, have really helped inform the kind of teacher I'd like to be." This fall, she will teach a weekly course at the Health Science Academy of the Arthur Ashe Institute for Urban Health.

"Sarah epitomizes the ideals of the David Rockefeller Fellowship," says Sidney Strickland, dean of graduate and postgraduate studies and vice president for educational affairs. "She is a superb scientist, committed to teaching and community service, and an interactive and friendly colleague."

Ms. Wacker was presented with the fellowship — established in 1995 by the university's alumni association — at this year's Convocation Luncheon on June 11. "I am so grateful to be honored with this award named for David Rockefeller, who has gone above and beyond to support this graduate program that is so important to all of us," says Ms. Wacker.

Following tradition, faculty mentors gave congratulatory tributes to this year's graduates. Printed here are the transcripts of those speeches, as they were read on June 11. Three members of the class of 2009 — Taulant Bacaj, Sarah Garrett Injac and Satoshi Yoshimura — were unable to attend the festivities. Students in the Tri-Institutional M.D.-Ph.D. Program are marked with an asterisk.

Sourabh Banerjee presented by Thomas P. Sakmar

B.Sc., St. Stephen's College, University of Delhi
M.Sc., Indian Institute of Technology
Studies of G Protein Coupled Receptors Incorporated into a Novel, Nanoscale, Membrane-mimetic System

Sourabh Banerjee joined my laboratory in 2004 as a graduate student in the Tri-Institutional Program in Chemical Biology. A native of India, Sourabh's earlier educational background and training were exceptional — St. Stephen's College and the India Institute of Technology in New Delhi. Coinciding roughly with Sourabh's arrival, I was becoming frustrated. Although we were making good progress studying a particular class of cell membrane receptors called heptahelicals, I was worried that we were missing the point. Our strategy was to remove the receptors from the membranes and purify them in detergents. The detergents used to purify the receptors are remarkably similar to ordinary household detergents and soaps: Like Scrubbing Bubbles, the lab detergents clean away everything but the receptors, which are proteins.

But we had more and more information that the protein receptors must interact with the lipids and fatty acids in the membrane bilayer to function normally. Receptors just don't like to be "squeaky clean." Sourabh took up the question of finding some new way to purify and study receptors without cleaning away the membrane lipids — not an easy problem. He scratched his head, went back to first principles and noted that our own bodies solved a similar problem when they evolved a class of proteins called lipoproteins, proteins that essentially wrap around lipids like a belt to form a kind of disc-like structure.

He went on to clone and characterize a novel lipoprotein gene and he used it to create what he called NABBs, or nanoscale apolipoprotein bound bilayers. He showed that he could rapidly purify heptahelical receptors using NABBs, and that the receptors, which were now trapped inside NABB nanoparticles, were stable and functioned normally. He even took snapshots of the NABBs with an electron microscope. Sourabh's new NABB technology will have a huge impact on studies of membrane receptors and channels, which are targets for nearly one-quarter of therapeutic drugs. At least 50 labs are now using NABBs, or some pirated version, and they might even make it to the research equivalent of mass production — namely, they might be available in a prepackaged kit. It is exceptional for a student to produce and validate a new technology.

On a personal note, Sourabh is the kind of rare individual who never seems to have a bad day — always enthusiastic, never complaining, always eager and energetic. Sourabh is also one of the most Web-connected people I know; he networks, Googles, blogs, posts, Twitters, profiles, streams, reviews and lists. He became a top-10 "CNN Newsmaker" in 2006 when he posted a live video feed of the small plane crash here in Manhattan on 72nd Street (many of you probably watched Sourabh's feed), and he was interviewed at length about his experience for the CNN Newsmakers annual awards show. Sourabh is now a postdoctoral fellow at Weill Cornell Medical College and he and his wife Mansi would like to make London their next stop.

Cameron D. Bess presented by Sanford M. Simon

B.S., University of California, Santa Cruz
Analysis of Cellular Factors Involved in Adeno-associated Virus Type 2 Entry

As an undergraduate at the University of California, Santa Cruz, where he studied yeast genetics, Cameron Bess was the first in his family to attend a university. We were fortunate to have Cameron Bess join the Rockefeller University graduate program and I was fortunate to have Cameron join my lab. Cameron is bright, thoughtful and has an incredible amount of energy. When Cameron joined my lab, we were not doing any work on viruses. Building on his experi-

ence in a lab rotation in Paul Bieniasz's lab, Cameron initiated what has become a very productive and enjoyable collaboration with Paul Bieniasz and Nolwenn Jouvenet studying the cell biology of viruses.

Without missing a beat in the lab, Cameron kept moving to a strong beat outside the lab. He has been a key figure in raising the knowledge and concern of all of us on campus about the consequences of the scientific pursuit on the world around us. I am a better person for having Cameron as a student and colleague and Rockefeller is a better place. Cameron is currently at the National Institutes of Health studying malaria.

You might never guess it from Cameron's shy, reserved style. But in college, he would sing and dance in musicals. Thus, in fitting tribute to a show he performed in, *West Side Story*:

To the tune of "Jet Song"

When you're a Bess
You're the best all the way
From your first Western blot
To your last cell assay.

When you're a Bess
Science projects fly through
You attack HIV
Then AAV2.

At UC Santa Cruz
You starred in *West Side Story*
You wore your dance shoes
The footlights and the glory
But then at Rockefeller
Your science it was stellar
Your thesis … a bestseller.

Work on a virus
Is tough and complex
Each answer you found
Led to three new projects.

When you're a Bess
If injustice is found
You grab your gang, Pugwash
You never back down.

A lab with a Bess
Will have laughs there's no doubt
Mixing science and fun
That's what you're all about.

You're now on new soil
Working on malaria
In Mali you toil
A most important area.

To the tune of "Gee, Officer Krupke"

Dear good doctor Cameron
You must understand
Some days science flies and soars
Some days it crash lands
Stay true to your vision
It's worth the good fight
You know you'd rather win than lose
But it's Bess to be right.

Kıvanç Birsoy presented by Jeffrey M. Friedman

B.S., Bilkent University
Transcriptional Regulation of Adipocyte Function

Michaelangelo described his craft as follows: "I saw the angel in the marble and carved until I set him free." This description well describes our experience as biologists. The marble is the mystery and wonder of life and the angel is the insights we glean and share with our colleagues. When embarking on a career in science, the excitement of this experience is boundless. Each new result, every new conclusion, all of our publications carry with them an elation that is hard to describe to those who have not experienced it. But with time, the novelty of each new result, conclusion or paper fades slightly, and the jubilation of each dims just a bit. But then something happens. To paraphrase Albert Schweitzer: In everyone's life at some time, our inner fire dims. It is then burst into full flame by an encounter with another human being. We should all be thankful for those people who rekindle our inner spirit. For me, that person is Kıvanç Birsoy.

Kıvanç hails from Turkey, where he received the highest scores nationally out of two million students on a standardized test given to all high school seniors. For this, he received a watch and a plaque from the president of Turkey; I'm sorry to tell you, Kıvanç, this will probably not measure up. His high school science project in plant biology was selected as being one of the 15 best in Turkey and this enabled him to enter the Biology Olympics, which I wasn't aware existed, where he won a medal. He was the first undergraduate at Bilkent University in Ankara to receive the president's prize there. He also published an independent paper as an undergraduate in Turkey during a three-week rotation in the UK. He also had the highest GRE scores possible when he applied to Rockefeller and was accepted without an interview, and I was quite naturally delighted when he joined my laboratory.

We study the regulation of body weight and a key question relates to the mechanisms by which fat cells increase their mass in obesity and decrease it in leanness. This requires that we understand the nature of the ensemble of factors that turn genes on and off in fat cells. It was this problem that Kıvanç undertook. Kıvanç has contributed to this greatly by identifying the earliest transcription factor required for fat cell formation. He also introduced the firefly luciferase protein into fat cells so that he could observe their transcriptional activity by measuring little bursts of light in living animals as a means for dissecting the transcriptional network that makes fat cells what they are. As if this wasn't enough, Kıvanç, working with another lab member, used these mice to identify fat, or adipocyte, stem cells, which was a major advance.

Seeing Kıvanç graduate is bittersweet. While it is clear that the time has come for him to move on in his career as a postdoctoral fellow with David Sabatini at MIT, I and the others in the lab will miss his intelligence, passion, cheerfulness, humor, drive and love of artisanal cocktails in hidden speakeasies around New York, which I must confess I helped introduce him to. In fact, at one point, we were literally concerned that he was going to go back to Istanbul to open a branch of the Milk & Honey cocktail franchise there. Despite the fact that Kıvanç is moving on, I will watch with great interest to see if he crafts more angels out of marble and then if, after a great long while, he has the great fortune of some day having the satisfaction of having someone like him rekindle his own flame.

Prabhjot Singh Dhadialla presented by Sidney Strickland

B.S., B.A., University of Rochester
A Role for Adult Stem Cells and Tumor Necrosis Factor in Peripheral Nerve Development

As science has accelerated the acquisition of information, the processing of this information has become a major challenge. How does one sort through reams of data to identify patterns and see the big picture? This problem intrigued Jot Dhadialla. He therefore collaborated with a student-colleague at Cornell to apply new mathematical methods to study molecules important for peripheral nerve development. Their method, with the impressive name of Maximum Entropy Network Analysis, showed for the first time that tumor necrosis factor, a well-known molecule in the immune system, is a critical player in nerve myelination. His work is important for the specific identification of a new molecule in nerve development, and also for the method he has developed, which can be applied to countless other systems.

Jot Dhadialla spent his boyhood days in East Africa. Ninety years ago, his family came from Punjab, India, to Kenya to help build the railroad, and much of his family still lives there. After graduating from the University of Rochester, he joined our M.D.-Ph.D. program. In addition to his affinity for basic science and medicine, he has been shaped by his African heritage to be extremely interested in science and social policy. Jot has spent the last few months in Kenya and will soon return to medical school to finish his medical degree. He is gifted in so many areas that it will be fascinating to see where his path takes him.

Nadya Dimitrova presented by Titia de Lange

Sc.B., Brown University
Characterization of a Novel 53BP1-dependent Mechanism That Promotes Nonhomologous End Joining of Deprotected Telomeres by Increasing Chromatin Mobility

Nadya Dimitrova was born and raised in Bulgaria. Like many former Soviet countries, Bulgaria delighted in the freedom gained after 1989, which allowed Nadya to study abroad. Nadya chose training in biology at Brown University and then came to the Rockefeller graduate program with two main interests: neurobiology and cancer biology. Her interest in neurobiology led her to work with Paul Greengard before she joined my lab in the summer of 2003 to work on cancer-related issues.

Nadya initially joined our efforts to understand how telomeres solve the end-protection problem, but her project dragged her to what was then still a fringe effort in the lab, to understand the fundamental principles of how cells detect DNA damage and how DNA lesions are repaired. In part through Nadya's work and her many journal club presentations in which she educated the lab (as well as her adviser) on this rapidly moving field, this issue is now a much more central aspect of our research.

Nadya's experiments focused on the function of a DNA damage response factor, 53BP1, which was known to accumulate at DNA breaks but whose function was not known. In an elegant series of experiments, Nadya discovered that 53BP1 endows broken DNA ends with the ability to move through the nucleus. This rapid movement, detected by Nadya using ingenious live-cell imaging experiments, provides a DNA break with a greater chance of encountering another DNA end so that it can be repaired. This introduced a completely new concept, that of DNA dynamics, into the DNA repair field. Nadya's efforts led to three papers, one in *Nature*, and more is in the pipeline.

Nadya's adventures in the DNA repair arena went so far outside the scope of the lab that there came a moment where I realized that rather than Nadya coming to me for advice, I was going to Nadya for guidance on issues relating to DNA damage response. At the same time, Nadya must have realized that I was no longer a reliable source of information and suggestions to her. This is, of course, the final rite of passage for a student: going beyond what the adviser knows or can intuit and moving into a new area, navigating on her own. I don't wish to give the impression that Nadya was isolated, though. While at the fringe scientifically, Nadya was at the center of the lab socially, at least in so far as the parties thrown by my lab can be said to have a center at all. I will miss that aspect of Nadya almost as much as her science. Although I must admit that I am a little relieved that there will be one less person at our parties trying to get me to drink more shots than I can handle.

Nadya defended her thesis in November 2008 and was honored earlier this year by the prestigious Harold Weintraub award. She has also received a Damon Runyon Postdoctoral Fellowship, which will support her current research in the lab of Tyler Jacks at Massachusetts Institute of Technology. In Tyler's lab, she has already repeated her trick of starting something entirely novel, and I wouldn't be surprised if Tyler finds himself going to Nadya for advice, just like I did, rather than vice versa.

Stefano Di Talia presented by Frederick R. Cross (on behalf of himself and Eric D. Siggia)

Laurea, University of Naples Federico II

Cell Size Control and Asymmetric Cell Fates in Start of the Saccharomyces Cerevisiae *Cell Cycle*

Stefano Di Talia came to Rockefeller with a strong background in physics. He chose to work on some classical questions in cell cycle control, jointly advised by me and by Eric Siggia. Stefano started out knowing very little biology, but he had great curiosity and an ability to apply a physical way of thinking to biological problems. Despite a rather self-deprecating demeanor and a somewhat slow start dealing with the vagaries of biological materials, he carried out an incisive series of experiments on the long-standing problem of cell size control. His standards for the quality and reliability of his biological work became highly rigorous, and he was absolutely persistent in learning whatever methods might be needed to take the next step. In the course of his Ph.D. work, he started as a person with good physics training and a general if unformed interest in biology, and came out as a committed and highly effective experimental cell biologist. Fortunately, he retained his physical way of thinking, which is quite different from most of what goes on in biology; this gave his experiments a valuable quantitative flavor and an interesting philosophical twist. Interdisciplinary scientists of Stefano's style will be very well equipped for 21st-century science. He has now taken his interests and approaches to the study of another long-standing classical problem, the interrelationship of cell cycle control and development, working in the laboratory of Eric Wieschaus at Princeton University, a Nobel Prize-winning fruit fly developmental geneticist.

Holger L.J. Dormann presented by C. David Allis

Diplom, Eberhard Karls University of Tübingen

Regulation of Heterochromatin Protein 1 by Phosphorylation of Histone H3 and the HP1 Hinge Domain

Holger Dormann came to the Allis laboratory as a well-trained cell biologist, having received his undergraduate training in Tübingen, including a diploma thesis carried out in Günter Blobel's laboratory. Working closely with a postdoc, Wolfgang Fischle, Holger and Wolfgang put forward and critically tested a new theory in histone biology — "phospho-methyl switching." Holger went on to extend these concepts beyond histone proteins, asking if switches also exist in non-histone proteins that "read" histone marks, notably a well-known heterochromatin-associated protein 1 (HP1). The chromatin field took early notice of Holger's talents, and early in his graduate career, Holger was awarded a prestigious Boehringer Ingelheim predoctoral fellowship to support his studies. But excellence in science is only one part of what makes Holger so special. How many graduate students can make the claim that they leave a lab with a scientific style named after them? Holger's clockwork precision and reputation for large-scale experiments, containing every conceivable control, forward and backward, has became known, at least in my lab, as being "Holgerian." Being Holgerian also means someone who would help you, day or night, no questions asked. He will be missed.

Without question, Holger's marriage marked one of the most notable "switches" of his Ph.D. career — a switch from bachelorhood to married life. But when Doro graduated ahead of Holger and began her postdoctoral studies in Munich, Holger faced an unexpected switch — a temporary switch back to bachelorhood. Spending long hours in the laboratory, Allis lab members worried that Holger would soon waste away, but Holger survived the calorie-burning chore of thesis writing, going on to give one of the more memorable thesis presentations. Yes you can. Switching again, Holger made the decision to pursue what we are sure will be a highly successful career in patent law. Said differently, no interaction, no matter how strong, can keep interacting partners apart; switching works inside and outside of science. It is in our genes; or is it our epigenes? We should all strive to be a little "Holgerian."

Ben Drapkin* presented by Frederick R. Cross

B.S., Yale University

Peak Mitotic Cyclin Permits Mitotic Exit

Ben Drapkin, a student in the M.D.-Ph.D. program, decided to carry out his Ph.D. work in my laboratory, with the aim of carrying out quantitative studies on the control of mitosis, the final step in cell division. Ben's work was most notably characterized by three features: first, rigorous accuracy in all his experiments, and second, an insistence on keeping the big picture in sight. These two things don't often fit together so well, since great accuracy frequently is accompanied by a complete loss of perspective on why it was so important to be accurate in the first place. The way Ben kept these things together relied on the third key characteristic of his work: almost superhuman persistence. He worked on a series of projects that were bedeviled with a truly remarkable series of misfortunes, including horrifying and bizarre artifacts, unreliable published information and just general lack of cooperation from the experimental system. These barriers would have stopped many people. But Ben was motivated not just to carry out some experiments, make some measurements and graduate; he was really interested in the biology, and he wanted to make a serious contribution to understanding it. His project was originally expected (at least by me) to confirm a comfortable, widely believed but untested theory of mitotic control. In the end Ben largely cut the legs from this theory, along the way providing a superior alternative. In doing so, he developed methods and posed problems that have provided approaches for several other graduate students in the laboratory. He is now going on to further medical training, where his rigorous approach will be further challenged by the vagaries not only of experimental research, but of work on human patients. As with his graduate work, I expect that the obvious difficulties of carrying out truly rigorous clinical research will be forced to yield to Ben's obdurate insistence on learning something important, and learning it right.

Elizabeth M. Duncan presented by C. David Allis

A.B., Dartmouth College

Regulated Histone H3 Proteolysis during Mouse Embryonic Stem Cell Differentiation

Elizabeth Duncan came to Rockefeller from Dartmouth College, where she graduated with honors (cum laude) in English and flirted with a possible career in medicine. However, after becoming hooked on research, Beth expressed an interest in studying chromatin biology and epigenetics in the context of mammalian development. While today marks a formal end to Beth's remarkable doctoral studies, it also marks a new beginning on what I am sure will be an even more successful postdoctoral journey. Ends and new beginnings also summarize Beth's remarkable research findings as she investigated the behavior of histone proteins during defined pathways of mouse embryonic stem cell differentiation. Beth determined that an oddly migrating band was in fact a "clipped" histone, pointing us and the chromatin field to a novel mechanism: proteolytical clipping of histones as a means to generate new ends that, in turn, alter a cell's epigenetic landscape as it differentiates. Beth then made the gutsy decision to purify the enzymatic activity responsible for generating the clipped histone end, and convincingly showed that it was an enzyme not linked to histone metabolism before. Succeeding in the cold room seemed to come as easily to Beth as breaking her personal bests in New York and Boston marathons. If "Just Do It" ever applied to a graduate student, Beth would be high on the list.

Lest you worry about Beth's mental health, she is well balanced. I attribute this, at least in part, to her daily morning jogs, which I came to realize Beth uses to clear her head, and often to think about her experiments, and more recently, her family. Beth is the real "OCTA-MOM" (eight copies of histones per nucleosome). I have no doubt that Beth will go on to run many more races and to do many more wonderful things, both inside and outside of science. The only real questions with Beth are how far and how fast will she go. The answers I keep getting are very far and very fast.

Robert R. Flavell* presented by Tom W. Muir

B.A., Wesleyan University

Novel Interactions of the Hormone Leptin Revealed by PET Imaging in Rodents and Rhesus Macaques

Rob Flavell has been associated with my lab since the fading days of the Clinton administration. A lot has happened since then. He graduated from Wesleyan, where he majored in math and chemistry, and he immediately joined my group as a research tech. He was extremely productive in this capacity; in fact, his output was equivalent to that of a first-rate grad student, and I guess Rob realized that he may as well become one. So it was that

he joined the M.D.-Ph.D. program in the fall of 2002. Though Rob is not the only lab tech in my lab to join the ranks of the Rockefeller grad student population, he is the only one who's come back to do his Ph.D. with me. And I'm not really sure what to make of this. I suspect that Rob's allegiance is in some way linked to a persistent rumor that I'm in possession of certain photographs documenting his outrageous behavior at a Muir lab holiday party in a Russian vodka bar in 2001. Rob, I must now tell you that I'm in possession of no such photographs.

At any rate, he joined my lab following his initial medical training and informed me that he wanted to work on biomedical imaging. This was somewhat problematic, since we did not work on biomedical imaging, which I presume he knew. Fortunately, his arrival coincided with some discussions I'd been having with Jeff Friedman on performing some engineering work on leptin. Rob quickly saw an opportunity and set off to develop some methodologies for performing PET imaging on leptin for use in various animal models of obesity. Rob had to solve many problems along the way. The biggest of these was how to attach the positron-emitting isotope fluorine-18 to the protein site-specifically and without destroying its function. Now we kind of knew how to do this using existing chemistries, but the reactions that we used were too slow compared to the very short half-life of the isotope. To solve this problem, Rob made use of an organo-catalytic process that allowed him to shorten the reaction time from several hours to a few seconds. With this new, generally useful protocol in place, Rob and his collaborators in the Friedman lab and the biomedical imaging center over at Weill Cornell performed a beautiful series of high-resolution PET imaging studies on leptin biodistribution in rodents as well as primates. This work has revealed how the hormone is cleared out of the body and suggests a novel mechanism of uptake into the brain. Rob has now returned to finish off his medical training, and I wouldn't be at all surprised if he returns to my lab for postdoctoral work. Particularly since I may be in possession of certain photographs detailing his escapades in the Far East.

Michael Gelfand* presented by A. James Hudspeth

B.S., M.S., Yale University

A Model of the Production of Spontaneous Otoacoustic Emission in the Tokay Gecko

It's my very considerable pleasure to recognize the incipient doctor, Michael Gelfand, who, like other members of our group works on the process of hearing. Now, as you all know, sounds are just vibrations in the ear. The external ear funnels those vibrations into the middle ear, where they oscillate three tiny bones: the hammer, the anvil and the stirrup. Finally, the vibrations reach the internal ear, or cochlea, where they're converted into electrical signals, which are the common currency of all of our nervous signaling. The cells that do the work are called hair cells; there are 16,000 of those in each of our cochleas. Each of these cells extends a little, tiny tuft of miniscule processes that vibrate in response to sound and then converts that mechanical information into an electrical signal that can then be forwarded to the brain. The remarkable fact is that these cells are not just passive recipients of sound, but instead, each hair cell is a little hearing aid, if you will. It actually can amplify its input several hundreds of times. When these cells wear out, we no longer can hear normally, we are hard of hearing. It is then necessary to use an electronic aid to supplement the process, to replace the biological hearing aid that came as original equipment.

Now just like this public address system, the ear's amplifier can be turned up too far, and if that happens, it begins to oscillate, just as this sound system would. Eighty-five percent of normal human ears can actually emit sound; sound is actually measureable coming out of the ear in a suitably quiet environment. Mike Gelfand has been studying how this comes about. What are the circumstances and what are the mechanisms by which this sound is produced? He's used geckos, which are the strange lizards that can climb along walls and ceilings, because their ears are particularly florid producers of these spontaneous oscillations. By making complicated mathematical models of the process, Mike has learned the nature of the processes that cause the oscillations to occur. And by that means, he has considerably advanced our understanding of the ear's remarkable amplifier. Mike's a student in the medical scientist training program, so he's also on his way to the M.D. degree at present. Because of his patience and his sincerity and especially his human warmth, he has the makings of a really fine physician as well as an astute researcher. So, though it remains to be seen which of these paths he'll pursue, my colleagues and I want to wish him the very best.

Elizabeth A. George Cisar presented by Tom W. Muir

B.S., The University of North Carolina, Chapel Hill

Mechanism of Signal Transduction by the Staphylococcus aureus *Quorum Sensing Receptor AgrC*

Elizabeth George Cisar joined our graduate program right out of high school. Prior to high school, she'd actually graduated from UNC Chapel Hill, with a degree in chemistry. Now if you're not already confused, Beth spent the first year of her high school up in Ithaca, New York, at Cornell before joining my lab in the summer of 2004. For her thesis, Beth studied how virulence is regulated in pathogenic staphylococcus bacteria through something called quorum sensing. So for the nonspecialist, staph in many ways act like soccer hooligans. When they're on their own, they're utterly docile and harmless, but get them in a crowd, particularly in the presence of the right chemical stimulant, and you'd better watch out. Indeed, staph turn on their very own response, the ability of the infection to spread, only when their numbers have reached a certain threshold, hence the term "quorum sensing."

So how does this work? Well, during her time here, Beth focused on the molecular language by which these bugs talk to each other. Using a combination of chemistry and genetic tools, Beth was able to listen in on their conversations and discovered something really quite unexpected, namely that the protein receptors involved in sensing the quorum operate through what she refers to as symmetrical signaling. Now this is really hard to explain, even to the aficionados, it turns out, but I'll try using the following analogy. Imagine you're looking at a mirror, and you put out your hand to touch your reflected image, only to find that the hand emerges from the mirror and touches you at the same time. Pretty weird stuff. When she first told me about this, I actually thought she'd spent too much time listening to bugs. But sure enough, Beth was right. Her work clearly showed that the receptor histidine kinase proteins that sense the quorum are paired up, and activation of just one component of the dimer automatically activates its partner. This, she believes, provides an amplification mechanism that drives the sensing process. Beth will shortly move out to The Scripps in La Jolla, where she will carry out postdoctoral studies, in a sense mirroring my own career path. She will move there with her husband Justin, who is also a student in the Tri-Institutional Chemical Biology Program — that's why they spent a year in Ithaca. And just one last thing. For those of you wondering how Beth could have obtained an undergraduate education before going to high school, she taught high school chemistry after going to UNC.

Doruk Gölcü presented by Charles D. Gilbert

B.S., Bilkent University

Perceptual Learning of Object Shape

Doruk Gölcü came to Rockefeller after receiving an undergraduate degree in the department of molecular biology and genetics at Bilkent University in Anakara, Turkey. Doruk's work at Rockefeller involved using psychophysical tools to study brain mechanisms of object recognition and perceptual learning. Psychophysics is the science of quantitative measurement of perception and behavior and is a valuable tool for understanding the way by which information is represented, or stored, in the brain. When thinking about how objects are represented, one could imagine that individual neurons could respond specifically to individual objects, representing them holistically. One theme supports this view, suggesting the existence of grandmother cells, where one cell would be selective for a single unique object. The alternative hypothesis is that objects are represented as a set of their component features. In this view the object would be represented by an ensemble of neurons, each responding specifically to different object components. Doruk's studies supported the latter idea, finding that learning to recognize one object transferred to other objects those shared components with the learned object.

Doruk is hoping to apply his experience in the study of the behavioral basis of human perception and cognition to other systems of animal behavior and neuroethology.

Doeke Romke Hekstra presented by Tom W. Muir (on behalf of Stanislas Leibler)

M.Sc., Leiden University

Population Dynamics in a Model Closed Ecosystem

Doeke Hekstra is an explorer of claustral ecology, a new field studying closed ecological systems. There are not many laboratories working in this field; there are no specialized journals and no conferences. Its potential applications range from biological support systems for voyages to Mars to small ecospheres that you can purchase from the American Museum of Natural History, in fact it was one of those ecospheres that inspired Doeke to

build his experiments. He enclosed inside small glass containers mixtures of three microbial species: algae, bacteria and ciliates, and then measured their dynamics over periods of months with second resolution. In the process of these studies, he notably found that algae transmit circadian rhythms to bacteria. To do this, he had to build his own microscopes from scratch and solve numerous problems of microbiology with optics and computer science. One thing you quickly learn about Doeke when you get to know him is that he's not only smart and curious, but he's fearless. If he'd lived in the 17th century, he would have become another Peter Stuyvesant, developing the settlement of New Amsterdam. Instead, he is exploring infinite worlds of closed ecosystems. Watch out: I would not be surprised if one day our grandchildren attend the Hekstra High School here in New York, or maybe in our colony on Mars.

Elizabeth Anne Heller presented by Nathaniel Heintz

B.A., University of Pennsylvania
Synaptic Protein Profiling in the Mammalian Brain

Elizabeth Heller came to Rockefeller with an interest in molecular mechanisms of nervous system function, having graduated Phi Beta Kappa from Penn. Liz had been conducting behavioral studies of learning and memory, and wished to expand her experimental range into the fields of mammalian genetics and biochemistry. It has been my experience here that the best students, and Liz certainly qualifies here, should be left to their own devices a bit. In their pursuit of a project that is sufficiently important to satisfy their curiosity and ambition, they almost always choose to break down the experimental barriers that have failed to yield thus far. Of course, Liz being Liz, she took this to an extreme! She sought to address one of the most difficult biochemical problems facing us today: defining the nature of the biochemical code that distinguishes one connection in the nervous system from all others. This sounds rather simple doesn't it? Just isolate the connections in question, called synapses, and determine their composition — no big deal! In fact, many laboratories have been working on this basic structure, identifying about 1,000 different proteins that are associated with it. So why bother?

Because, of course, there is a catch! You see, there are hundreds of varieties of these synapses, and information processing in the brain is dependent on maintaining these varieties and ensuring that they function properly. What Liz and her colleagues did was to develop an ingenious approach for studying the biochemistry of just one of these varieties at a time. This was no small feat, a bit like taking a ton of fruit salad and figuring out a way to isolate and savor the flavors of only that rare boysenberry sitting at the bottom of the bowl! Liz then took this approach, which we have referred to as synaptic protein profiling, and used it to provide the first biochemical glimpse of the elusive GABAergic synapse, demonstrating that its complex and critical roles in the brain are endowed to it by a relatively simple collection of proteins. As I hope you can appreciate from these comments, Liz has been instrumental in breaching a barrier that has faced our field for decades, and her studies are certain to stand tall among other efforts to understand the biochemical nature of synapse specificity.

In closing, I would just like to say to complement her deep intelligence, Liz is endowed with a tremendous sense of humor and a serious will to succeed. It has been a privilege for me to serve as her mentor, and it will be a pleasure to watch her as she becomes the scientific force that is her destiny. She is the only student for whom I have written a one-sentence letter of recommendation — which was a great success!

"I want you to know that if you do not interview Liz Heller and hire her, you are an idiot!"

Jessica Howell presented by Markus Stoffel

B.A., University of Pennsylvania
Mechanistic and Physiological Studies of the Insulin-dependent Regulation of Foxa2

Jessica Howell joined my lab in 2005. She came well prepared for her Ph.D. work, having graduated from U Penn and worked in the laboratory of another Rockefeller graduate. Jessica decided to work on my favorite project, a transcription factor called Foxa2 that has a history here at Rockefeller. It was originally identified by Jim Darnell, who showed that this factor is important for liver-specific gene expression, and the first structure of the DNA binding domain of Foxa2 was determined by Stephen Burley in the late '80s when he was here.

We recently discovered that in the liver, Foxa2 acts as a sensor, and that it integrates lipid metabolism in the fasted and fed states. In the fasted state, Foxa2 is active and regulates the expression of genes that burn fat or produce ketone bodies that are utilized by other tissues. In the fed state, when energy sources abandon and insulin levels rise, Foxa2 is inactivated through phosphorylation and nuclear exclusion. Jessica investigated the molecular mechanism by which the activity of Foxa2 is regulated. She identified the machinery that is responsible for shuttling Foxa2 in and out of the nucleus and a specific domain that mediates the export of Foxa2 from the nucleus to the cytoplasm. She showed that mutations in this domain prevented Foxa2 from being exported from the nucleus and that it can still be regulated by insulin signaling. She also participated in studies that revealed that Foxa2 regulates two important neuropeptides in the brain: melanin-concentrating hormone and orexin, which stimulate appetite and alertness and food-seeking behavior during fasting. These studies uncovered that Foxa2 acts as a metabolic sensor in neurons of the hypothalamus to integrate metabolic signals, adaptive behavior and physiological responses.

In 2006, I decided to take a position at the ETH, Zurich. To my delight, Jessica decided to join the lab in this journey and continue her studies in Switzerland. This move was not always easy for Jessica, since that meant leaving family and close friends behind. But Jessica quickly adapted to the new environment, with the exception of the new time zone, which resulted in her working very late hours in the lab. Jessica also learned to like Bircher muesli, Swiss cheese and Lindt chocolates. Conversely, she introduced her colleagues to fine American foods, such as Hershey brownies and marshmallows. Jessica also took advantage of living in Central Europe by visiting many European countries and major cities; she even learned a modicum of Switzerdeutsche, which is a funny German accent that I cannot speak. Jessica will finish up her work in Zurich and work as a postdoctoral fellow and enjoy Swiss postdoctoral salaries for a few months before returning to the States in the fall to interview for academic positions and prepare for her wedding. I don't know in which order she will do this. I do know, however, that Jessica will have a bright future in science, and I wish her the best of luck in her personal and professional life.

Kuo-Chiang Hsia presented by André Hoelz (on behalf of Günter Blobel)

B.S., Fu Jen Catholic University
M.S., National Yang-Ming University
Architecture of a Coat for the Nuclear Pore Membrane

Kuo was born in Taiwan. He received a master of science degree from the National Yang-Ming University in Taipei in 2000 and continued to work there until he entered our graduate program in 2005.

Kuo came here well prepared with half a dozen excellent publications in the field of x-ray crystallography to his credit. He continued in this field when he joined our laboratory in 2005, taking on the nuclear pore complex (NPC). Solving the atomic structure of the entire NPC — a humongous and very dynamic protein assembly at the interface between the cytoplasm and the nucleus — is, for many reasons, impossible with present technology. Our laboratory embarked on an approach to solve the structure of bits in the hope to eventually piece them together. Kuo provided critical support on the feasibility of this approach. In a tour de force, he solved the structure of two interacting nucleoporins. The data allowed us not only to make predictions on the structure of a related pair of nucleoporins, but also led to the proposal of a model of how those proteins might be arranged in the context of the NPC. This work was published in *Cell*. Kuo's subsequent work then solved the structure of the related pair of nucleoporins and further substantiated the suggestion of the proposed context model. This work was published in *Molecular Cell*. Emboldened by his success, Kuo is now trying to crystallize much larger bits of the NPC, and in doing so, decided to continue to stay in our laboratory as a postdoctoral fellow.

While a graduate student here, Kuo married and became the father of two lovely children. His wife is a graduate student at Mount Sinai School of Medicine. I don't know how both of them keep this extraordinary pace, but obviously they do very well!

Martin Kampmann presented by Sanford M. Simon (on behalf of Günter Blobel)

M.A., University of Cambridge
Biophysical Characterization of Structure and Dynamics of Nuclear Pore Complex Components

Martin was born in Germany, received his undergraduate education at the University of Marburg, Germany, and then obtained a master's degree from Cambridge University, United Kingdom.

Martin entered the Rockefeller graduate program in 2003 with an exceptionally wide interest in the biological sciences that had been well nurtured by a remarkably broad exposure to the practice and thinking in several fields of biology. While he was a gradu-

ate student in our laboratory, he published two single-author papers in fields that were not principal to his thesis work. Attesting to his exceptional talent for rapid acquisition of expertise in a field new for him, he managed to complete the main body of his thesis work in little more than a year! Using electron microscopical analyses and single particle image reconstruction methods, he described the three-dimensional structure of a heptameric membrane coating module that is part of the outer layer of the huge nuclear pore complex. He succeeded in fitting in structures of those members of the heptamer that had so far been determined at atomic resolutions. This work was recently published in *Nature Structural and Molecular Biology*.

In addition to his many laboratory projects, he founded and organized the Yeast Club at Rockefeller. This forum serves to promote scientific exchange between students, postdocs and invited speakers. Moreover, he volunteers with New York Cares and the Science Room of the Harlem Children's Zone Literacy Workshop. In 2006, he received the prestigious David Rockefeller Fellowship.

Martin is going to stay in the laboratory to follow some promising lines of research that he pursued here and that are relevant to his thesis work and then will move on to his postdoctoral training at the University of California, San Francisco.

Erica C. Keen* presented by A. James Hudspeth

B.S., Yale University

Transfer Properties of the Hair Cell-afferent Fiber Synapse

I'm now honored and delighted to recognize the nascent doctor Erica Corinne Keen, who's also carried out her research on the hearing process. Now I earlier introduced hair cells, which are the sensory receptors of the internal ear, and mentioned that each of these detects vibrations stemming from sound and produces an electrical response. For that response to be perceived, somehow the information has to be forwarded into the brain, and Erica studied how this comes about. More specifically, she was able to record electrical signals simultaneously from one of these receptive hair cells and from the afferent nerve fiber that connects it to the brain, and by that means she was able to show how hair cells transmit information.

The mills of neurophysiology grind exceeding fine, but they also grind very slow. Every experimental fact must be established with living organs and living cells and the most difficult aspect of such research is learning how to make an experimental operation, to take a bit of tissue out of the body, keep it alive during the experimentation and convince it somehow to reveal the answer to an interesting question. And it's in this realm that Erica has made a really singular contribution. She was the first to demonstrate how one could investigate the flow of information from a hair cell to the associated nerve fibers. Developing a new preparation like this is something like finding a new kind of art — Impressionism, Cubism or whatever; it gives you a new way of seeing things, a means of studying phenomena of which we weren't previously even aware.

Erica's approach is now being adopted by other groups around the world, which is testament to the fact that her pathbreaking work was quite important. Erica's presently engaged in her clinical work as part of the M.D.-Ph.D. degree program, and her success in this realm poses additional problems. She must decide in the next five months or so whether to continue on in the clinical endeavor or to return to basic research or perhaps find some combination of the two. My colleagues and I have enormously enjoyed working with Erica. We wish her the greatest success in whichever path she selects — as long as it's research.

Evan Zane Macosko* presented by Cori Bargmann

A.B., Harvard College

The Neural Circuitry of Social Behavior in Caenorhabditis elegans

Evan Zane Macosko, from the Tri-Institutional M.D.-Ph.D. Program, is a New Yorker, a Harvard graduate, a musician, a poet, a political idealist and a Renaissance man. With his education, Evan knew that in the 18th and 19th centuries, a debate raged among European philosophers on the proper balance between the rights of the individual and the needs of society. Opposing viewpoints were informed by opposing views of human nature as fundamentally good or flawed. On the utopian side, a vision of the perfect society was expressed by Jean-Jacques Rousseau in his essay *The Social Contract*:

"Each man, in giving himself to all, gives himself to nobody; and as there is no associate over whom he does not acquire the same right as he yields others over himself, he gains an equivalent for everything he loses, and an increase of force for the preservation of what he has."

As an idealist, Evan used his Ph.D. research to study just such a perfect society. Broadening the philosophical debate, he studied a society not of humans but of nematode roundworms called *Caenorhabditis elegans*. Within its small world, *C. elegans* enacts the spectrum of viewpoints expressed by European philosophers. They are free: Different worms, armed with distinct genotypes, choose between social or individualistic lifestyles. They are flexible: Changes in the environment scatter the social groups to the four corners of their round plates. Further changes allow new groups to form.

Evan, in his thesis work, defined the fundamental brain circuitry at the heart of these decisions. By tracking the genetic variation that makes individuals solitary or social, he identified a single pair of neurons that form the hub of the worm's social brain. Genes, environment, stress and signals from other animals converge on this neuronal hub. What emerges from the hub is a decision, switching the animal between attraction to other animals and repulsion from them.

In a dazzling set of experiments, Evan activated neurons and silenced them; shut some lines of neuronal communication while leaving other lines open; watched the neurons signal; and watched the worm's brain think as it responded to other worms. Evan's work shows how a fixed brain can generate flexible behaviors by allowing information to flow down alternative synaptic pathways. This idea of flexible remodeling has explanatory power in complex nervous systems as well as simple ones.

These experiments were only some of Evan's numerous accomplishments. In his imaginative and wide-ranging thesis work, he opened many avenues of research into animal social behaviors. Evan is now completing his M.D., but we look forward to the return of his remarkable creative intelligence to the world of research.

Trudy M. McCall presented by Bruce S. McEwen

B.S., University of California, Irvine

The Manipulation of Apical Dendritic Plasticity and the Consequences for the Effects of Chronic Stress

Trudy McCall graduated from the University of Calfornia, Irvine, in 2001, majoring in neuroscience. At UC Irvine, Trudy became interested in learning and memory, working with a leading figure in this area, James McGaugh, and she developed an interest in the hippocampus, a brain region that plays a key role in contextual and spatial memory. She won an Excellence in Research Award in her senior year. Trudy then worked for a year as academic coordinator for the neurobiology and behavior department at UC Irvine until she applied to and entered the Rockefeller graduate program in 2002.

Trudy joined our lab to work on the hippocampus, which we have found is a target of stress and stress hormones. Neurons have dendrites and dendrites are the "tree branches" of a neuron that receives input from other nerve cells. And neurons in the hippocampus have dendrites that shrink and lose connections as a result of chronic stress. Trudy chose to study the mechanism by which chronic stress causes the retraction of dendrites and impairs learning. She wanted to see whether she could prevent this dendritic retraction by disrupting a cell-surface molecule that is found on nerve cells, such as those in the hippocampus, that are able to expand or contract their dendritic trees as a result of stimulation. Trudy used a purified enzyme, called EndoN, that removes polysialic acid from the "neural cell adhesion molecule," a key molecule on the surface of neurons.

What Trudy found was somewhat of a surprise: Indeed, EndoN did partially prevent the effects of stress. The dendrites of stressed EndoN-treated animals were longer than those of stressed control animals, but they were also longer than those of control animals not treated with EndoN. That is, EndoN caused dendrites to become longer and more branched than normal, whether or not there was stress applied. And there was a reflection of this in the animals' behavior after chronic stress. While chronic stress causes a significant, but moderate, increase in anxiety and aggressive behavior, EndoN-treated rats that were also stressed showed a much larger increase in their anxiety and aggression. This suggests that the adaptive processes that occur during chronic stress normally dampen the behavioral changes that take place. Trudy is involved in a further study to find out whether the EndoN treatment makes the stressed animals more vulnerable to temporal lobe seizures and the damage that occurs in the hippocampus as a result of those seizures.

Melissa Noel presented by Sidney Strickland

B.S., University of Puerto Rico, Río Piedras

Novel Roles for the Tissue Plasminogen Activator System in the Development of Fetal Alcohol Syndrome and the Regulation of Contextual Learning after Stress

Fetal alcohol syndrome (FAS) is the most prevalent birth defect by a large margin. It occurs when a pregnant woman abuses alcohol during the last trimester. It affects one in 500 births and can cause neuronal loss in the brain and lifelong disabilities. In spite of its prevalence, little is known about why alcohol at this critical time is so damaging to the brain. Melissa Noel studied this syndrome. She used a mouse model of FAS consisting of exposing newborn mice to alcohol. She then showed that the protease tissue plasminogen activator plays a critical role in neuronal death. After alcohol exposure, control mice had massive neuronal death, but newborn mice that lack tPA had only one percent neu-

ronal loss. She has identified a new pathway involved in alcohol-mediated neuronal death and provided new avenues to design therapeutic approaches to alleviate FAS.

Melissa was born and raised in Puerto Rico. She first came to Rockefeller as a summer student in Bruce McEwen's lab and then returned as a graduate student. Through hard work and intelligence, she has done an extremely important thesis. Melissa epitomizes the growth that one sees in the best students, from her early days as a talented but beginning scientist to a mature investigator with the drive and independence to forge her own path. Melissa is continuing her training as a postdoc at Mount Sinai School of Medicine.

Jonathan Nowak* presented by Elaine Fuchs

B.A., The University of Chicago

Specification and Function of Early Hair Follicle Stem Cells

Jonathan Nowak received his B.A. from The University of Chicago with majors in biology and economics. We now celebrate his completion of the Ph.D. program at The Rockefeller University and, in the coming year, his M.D. at Weill Cornell Medical College. So do the degrees define the person? In Jonathan's case, they do. Jonathan has far-reaching interests and has displayed a genuine desire to learn and explore the intellectual depths that underlie each of his degrees. I've witnessed this first-hand while serving as his mentor through his successful Ph.D. thesis on the transcriptional control of epithelial differentiation and stem cell maintenance.

Jonathan came to my lab with a clear interest in stem cell biology. During his studies, he identified changes in the expression of the "Sox" family of transcription factors. When hair follicle stem cells switch from a resting to growing state, they turn off one Sox gene and turn on another. For his thesis research, he showed that this switch is important to our understanding of how stem cells regulate when to remain dormant, when to make hair and skin and when to repair wounds.

Jonathan's important discoveries were published in two papers, one in *Genes & Development* and the other in *Cell Stem Cell*. His major paper is likely to be a landmark in the field, lasting long after this wonderful day in which he is honored with a degree that recognizes these accomplishments.

Jonathan brings intellectual brain power, a quickness of mind, excellent bench skills and a wonderful enthusiasm to everything that he does. Finally, I would be remiss if I didn't mention that Jonathan relishes challenges that go beyond those that relate to his career. His honeymoon in the last year of his thesis research was not to Niagara Falls or Hawaii, but rather to the glaciers and frontiers of Tierra del Fuego. I've cherished the opportunity to witness this rising star in action.

Justin C. Paul* presented by Sidney Strickland

B.A., The Johns Hopkins University

Fibrin Formation and Dissolution in the Progression of Amyloid-β Pathology in Alzheimer's Disease

Alzheimer's disease, first characterized about 100 years ago in Germany, is a scourge of old age. This disease destroys short-term memory, and without the ability to form and retain memories, humans are empty shells. Thousands of labs work on AD, but it is still not known why neuronal cells die. Justin Paul studied this disease by using mouse models that develop Alzheimer's. He has beautifully shown that blood flow and blood clotting play a prominent role in the disease in mice. One of the most exciting aspects of his work is that it suggests a new mechanism for Alzheimer's and new therapeutic approaches that could ameliorate the disease.

Justin was born and raised in Boston. He inherits his interest in science and medicine from his family: His father and mother were both trained as chemists. After an outstanding undergraduate career at Johns Hopkins, he joined our M.D.-Ph.D. program. He is a fearless and creative scientist, and a warm and friendly colleague. He is now back in medical school finishing his medical degree. His appetite for science is matched by his appetite for food. He was renowned in our lab for finishing any and all leftovers at our weekly lab lunches.

Valentin Piëch presented by George N. Reeke Jr. (on behalf of himself and Charles D. Gilbert)

M.Sc., Swiss Federal Institute of Technology Zürich

Perceptual Learning, Long-range Horizontal Connections and Top-Down Influences in Primary Visual Cortex

Computational neuroscience attempts to construct computer models of things brains do to help us understand the relationships between perception, behavior and the fine details physiologists can study. Valentin Piëch's thesis is of a kind that I believe is essential preparation for contributing new advances in this area. He got hands-on experience with some very interesting experiments in Charles Gilbert's lab that showed how the demands of performing a particular task can change the way cells in the visual cortex respond to stimuli, and then he came to my lab and constructed a complex computer simulation that includes detailed elements of cortical circuitry. It provides a biologically realistic explanation, at the circuit level, of how these adaptive changes in response come about.

Valentin is one of the most thorough scientists I have ever met. I have time for just one anecdote to illustrate this. Part of his thesis project involved functional magnetic resonance imaging, or MRI, studies to look for effects in humans similar to those he had already studied in animals. He came to me one day and said, "These images don't look right." I had no idea what was wrong, but he spent a couple of weeks inventing some new statistical techniques to analyze those images, and then came back to tell me, "The technician set one of the dials wrong on the MRI machine." While he could not undo the damage that had been done, this work resulted in a paper with the MRI physicists explaining his new way to analyze images.

He demonstrated that his model was stable using dynamical systems theory methods that are pretty much new to many neuroscientists. His model ran too slowly on normal desktop computers, so he figured out how to run his code on one of those fast graphics processors that are sold for running computer games. And finally, he demonstrated that his model worked, not by applying it to the usual simple geometric figures, but by applying it to a real image, a picture of a *Playboy* Playmate much beloved of artificial vision researchers.

With these successes in hand, and with his thorough approach to every problem he encounters, I know Valentin will be successful in whatever he undertakes.

Andrew James Schile presented by Hermann Steller

B.S., Harvey Mudd College

Regulation of Apoptosis by XIAP Ubiquitin Ligase Activity

Andy's exceptional as a student in a number of ways, highly courageous, very independent, and very determined, and he came to my lab to investigate the regulation of programmed cell death in the mouse. All our cells have the ability to self-destruct when they are no longer needed by activating an intrinsic cell suicide program. And obviously the proper regulation of this program, termed apoptosis, is very important for normal development and tissue homeostasis and it plays a critical role in a variety of diseases. For example, if you have too little apoptosis, you are predisposed to have cancer and if there is too much cell death, it's associated with a wide variety of diseases including neurodegenerative diseases.

Now a major unresolved question in the field still is how it is exactly that cells make the decision between life and death and how they can at the spur of a moment activate that cell suicide program. This is particularly fascinating in the sense that all the components that are needed to carry out the cell suicide are expressed in our cells at all times, so very powerful inhibitory mechanisms must exist to make sure that this process is not inappropriately started. Now this is a question that Andy addressed in his thesis research, and particularly he investigated the mechanism by which a death-inhibitory protein, termed an inhibitor of apoptosis protein, or IAP, is used to regulate cell death. For this purpose, Andy generated mouse mutants that lacked either the entire gene or specific domains of it and examined the physiological role that this gene plays in the cell death of the mouse and in a tumor model. What Andy found and, actually for the first time showed in this way, was the physiological role of one particular IAP called X-linked IAP, or XIAP, in the mouse and that this is directly regulating the key executioners of cell death, the caspases, and that its need is to limit the productivity of these killer proteases. Importantly, when you inactivate XIAP, it actually protects mice against the emergence of tumors in tumor model and is particularly used to study this in lymphoma model. This is very relevant for all the efforts that are currently under way that target IAPs in kinds of therapy. IAPs are commonly overexpressed in human cancer and they've become very attractive drug targets in designing new cancer therapeutics, and the mice that Andy's generated are really critical in leading and guiding clinical trials for this new class of cancer therapeutics.

Moreover, the work that Andy's conducted has really radically changed the view of exactly how IAPs keep the caspases, the key killer proteases, off because he has shown that these IAPs act to attach a small protein called ubiquitin to the caspase and that is directly inhibiting caspases. So this work, which was really quite groundbreaking, was published last year in *Genes & Development* and since Andy graduated last year, he went on to the Jackson Laboratories, where he continues to reverse-engineer mice, and I'm sure he'll have a very bright future ahead.

Mark Schroeder presented by Ulrike Gaul

B.S., Cornell University

Hierarchy and Cis Regulation in Drosophila *Segmentation: Rules for Pattern Formation and Clues to Evolution*

It is a great pleasure to present Mark Schroeder as a graduate today. Mark is one of the few and the brave who seek to bridge the divide between computation and experiment, which we know is not an easy task. He came to my lab with a strong background in bioinformatics but with the explicit wish to combine in silico and in vivo methods to study the transcription control of pattern formation in the *Drosophila* embryo. And he proceeded to do nothing less than rewrite the textbook on a key paradigm of developmental biology.

The regulation of gene expression lies at the core of animal development. For example, the segmented body plan of the fly is set up in the early embryo by a hierarchically organized network of transcription factors that subdivides the embryo into increasingly smaller and sharper domains of expression. How is the patterning information encoded in this system and how is it unfolded? The problem had attracted a lot of attention when the participating genes were first discovered, but the effort waned in the 1990s, due to the limitations of the extant experimental approaches. With the sequencing of the *Drosophila* genome, computational approaches became feasible and Mark decided to take another look. Adapting an algorithm developed in collaboration with Eric Siggia's group, which searches genomic sequence for clusters of transcription factor binding sites, Mark identified some 25 new regulatory elements that drive expression in different regions of the embryo. When he analyzed the now vastly expanded set of regulatory elements, Mark discovered basic rules governing their composition and thereby laid the groundwork for our effort to predict expression patterns from the regulatory sequence. For the second part of his thesis, Mark decided to delve further into the biology of segmentation and to dissect the fascinating transition from nonperiodic to periodic patterns in the network. Using a diverse arsenal of methods, Mark showed that control by the maternal and gap factors reaches much deeper into the hierarchy than previously thought, and that the received classification of pair rule genes has to be revised.

Mark's work provides a great example of a productive integration of computation and experiment. His success rests on a rare combination of biological understanding, technical skill and creativity that he brought to the task. Mark has a remarkable ability to look at a question from all sides, to dig deeper and to think outside the box, which allowed him to devise smart new ways to probe his data and visualize the results, and to see things that nobody had ever noticed before. This ability is in fact so well developed that it sometimes took strenuous effort to bring Mark back near the box, let alone into the box. One of Mark's specialities in group meeting was to come up with real clever yet Byzantine experiments that would definitely resolve the posited question, only with the slight drawback that it would take forever. Such flights of imagination would be greeted by more or less gentle teasing, which Mark endured with good humor. All of us, however, cherish him as an incisive discussant with near-infinite curiosity and great nimbleness in critically following scientific questions well outside his immediate area of expertise.

Nicolai Siegel presented by George A.M. Cross

Sc.B., Brown University

Regulation of Gene Expression in Trypanosoma brucei

Nicolai become interested in the pathology of parasitic diseases after a 1997 visit to Bolivia, where Chagas disease, caused by *Trypanosoma cruzi*, was endemic. After high school he returned to Bolivia for a 15-month period of civil service, teaching in an orphanage in lieu of military service in Germany.

I met Nicolai after his junior year at Brown University, when he was admitted to the 2002 Summer Undergraduate Research Fellowship program. I told him that it should be possible to get a publishable piece of work out of the project I had in mind. Just one of those three-month projects that advisers think up without thinking through all the issues, but that, through Nicolai's insights and attention to detail, became a major piece of work whose main substance had to await Nicolai's acceptance into the graduate program in 2003. Although this was a groundbreaking piece of work, there were to be more of the same, aimed at understanding the very nonmainstream ways that trypanosomes regulate gene expression, most recently a cover article in *Genes & Development* that was also singled out for the highlights sections of *Science* magazine and elsewhere, and widely lauded in the field, resulting in many requests to Nicolai for advice and collaborations.

Nicolai's six-year association with my lab has been extraordinarily innovative and productive. Sadly he will be my last student, but it's nice for me to go out on such a high note. Following the example of his predecessor, Nicolai also found time to run the 2006 New York City Marathon in a very respectable 3 hours, 20 minutes. Nicolai will stay a couple of months to tidy up loose ends for one or two more papers, then spend three months traveling in South America before moving to the Pasteur Institute in Paris, where he will study the malaria parasite: a big loss for the trypanosome field, to which I hope he will eventually return. Nicolai, I thank you for your many contributions to the lab and we all wish you great success in the future.

Duncan Smith presented by M. Magda Konarska

B.A., University of Cambridge

The Role and Fate of Branch Site-U2 snRNA Pairing during Pre-messenger RNA Splicing

From the very first day when Duncan came to my lab I was certain that he would not be an easy student to mentor, and I was equally certain that mentoring him would be more than worth the effort. Now I can say that my first impression turned out to be completely correct: Duncan would never shy away from a challenging question in science or accept an easy way out of a difficult conceptual problem in his work; he would always demand a serious consideration of issues and come up with a beautiful, complete, always interesting interpretation of the data.

In the end, I wonder who benefited more from Duncan's stay in the lab — him or me? I know that his consistently serious attitude to science forced me to reconsider and reconfirm the reasons for my own commitment to science. Once in a while it may be a healthy exercise for every scientist.

Since Duncan left our lab already a week ago, I do not have to guess, I can say for sure that we all miss him a lot — his thoughtful advice, great conversations and great experiments — and we wish him all the very best in his scientific adventure across the street.

Joanna Louise Spencer* presented by Bruce S. McEwen

B.A., Yale University

Physiological Effects of Estradiol in the Mouse Hippocampal Formation

Joanna Spencer graduated from Yale in 2003 and entered the Tri-Institutional M.D.-Ph.D. Program in that same year. In her application to the program, she expressed an interest in doing research on "cancer or neurodegenerative diseases," but she also wrote that "my interest in signaling molecules was piqued during my junior year by discussions of reproductive endocrinology in a biology of reproduction course at Yale." Little did she realize that this latter statement would be prophetic, since her Ph.D. thesis deals with signaling molecules in the brain that mediate the actions of the hormone estradiol on processes in the hippocampus that are involved in synapse formation, memory and protection of nerve cells from damage.

Joanna's thesis research was based upon two lines of work in our laboratory: first, the discovery that estradiol, as well as other steroid hormones, not only works via receptors in the cell nucleus that regulate gene expression, but also acts near the cell surface and in the cytoplasm to cause chemical changes on molecules that stimulate (i.e., signal) key cellular events such as protein synthesis, neurotransmitter release, reorganization of the cytoskeleton and synapse formation; second, the finding that these "nongenomic" actions of estradiol and the receptors that mediate them exist in many, if not most, areas of the brain, including brain regions like the hippocampus that are involved in cognitive function as well as mood. Indeed, we previously discovered that estradiol stimulates the formation of new synaptic connections in the hippocampus of the female brain.

What Joanna accomplished, working with postdoctoral fellow Elizabeth Waters and with our collaborator at Weill Cornell Medical College, Teresa Milner, was two-fold. First, she established the role of estradiol in a mouse model in regulating two key signaling pathways: one, called Akt, that is linked to neuroprotection and also to protein synthesis; and the other, the TrkB receptor, that is linked to neuroprotection as well as structural changes such as synapse formation. Joanna went on to study a common human genetic variant in the molecule BDNF, which stimulates the TrkB receptor. To do this, she used a mouse model established by another Weill Cornell scientist, Francis Lee. In strains of mice carrying one or the other of the two genetic variants of BDNF, Joanna found that while estradiol was effective in stimulating the signaling pathways in both genotypes, there were important differences in how these pathways operated during the natural ovarian cycle, including the level of anxiety and memory functions that these two strains of mice displayed. Both differences recapitulate some of the features of mood and memory functions in women with the two genetic variants of BDNF. These findings are attacting considerable attention and being applied by scientists at the National Institute of Mental Health to better understand premenstrual mood disorders.

Till Strowig presented by Christian Münz

M.Sc., Technical University of Berlin

Of Mice and Men: Studying Innate and Adaptive Immunity against the Epstein-Barr Virus

Mens sana in corpore sano. A healthy mind in a healthy body. This Latin proverb describes Till's lifestyle, balancing intellectual challenge with his enthusiasm for sports. With his mind, Till has contributed to solving an essential problem in immunology, namely how one can study immune responses to pathogens that infect only humans. He has developed a mouse model, in which a functional human immune system develops from human blood stem cells. This allowed him to study human immune responses to the tumor virus Epstein-Barr virus in vivo, and will significantly change our design of preclinical studies for the treatment of human infectious diseases and cancers.

In parallel he has immersed himself in American sports. Being a fervent runner and marathon man, he has also followed baseball, basketball and American football intensely during the four years of his Ph.D. thesis. Like so many native New Yorkers, he has become a Yankees fan. Only the soccer World Cup 2006 in his home country Germany was able to briefly lure him back to European sports. I have no doubt that Till will continue to make his way, balancing science with sports, when he now continues his career in the immunobiology department of Yale University. Till, we look forward to many more exciting research results from you.

Grace Teng presented by F. Nina Papavasiliou

B.S., Yale University

Regulation of Immunoglobulin Gene Diversification by Noncoding RNAs

Our dean is fond of saying that overall, the best predictor for success during the sometimes grueling Ph.D. years is one's love for cooking. Grace is a phenomenal cook, so in retrospect, her steep trajectory in science was predictable.

Grace came to the lab five years ago, with an interest in how noncoding RNAs influence the flow of genetic information. Now if you open a textbook on this, you learn that the flow is linear: DNA makes RNA makes protein (with a little loop to account for reverse transcription). Of course, this almost linear view is rapidly becoming antiquated, a fact that Grace recognized very early and captured perfectly with the following analogy. In the sandwich that is this view of the central dogma of molecular biology, RNA is in the middle, and like with every good sandwich, it's what's in the middle that matters!

I count myself lucky then, that this young woman decided that the process we study in my lab, which is how immune cells generate antibodies, offered a decent kitchen in which to test her ideas about RNA. In her time in the lab, Grace has been persistent, creative and adventurous with her experiments. The fruits of her labor were published prominently last year, in a paper where she provides the first direct demonstration of how a tiny RNA can act not as a "fine-tuner," but rather as a prominent regulator of the expression of a DNA mutator, which is required for the generation of antibody diversity.

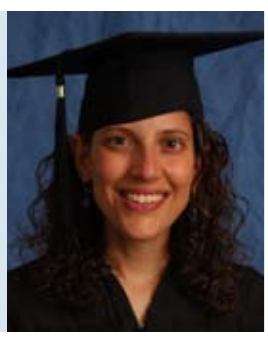
This paper carries both our names, mine for providing the ingredients and kitchen space, and hers for just about everything else, including the writing (she's a phenomenal writer as well).

Grace is planning to continue her work in the world of RNAs and gene regulation but will now switch her focus from microRNAs to the longest noncoding RNAs. I'm confident that in a few short years Grace will be starting up her own shop, but not before she does one last apprenticeship. In July, Grace is moving to New Haven, to continue her adventures in the laboratory of David Schatz at Yale University Medical School.

Jaclyn E. Tetenbaum-Novatt presented by Michael P. Rout

B.A., M.S., Brandeis University

Biochemical Analysis of the Protein-Protein Interactions Involved in Karyopherin-mediated Transport across the Nuclear Pore Complex



Jackie is a local-grown New Yorker who is a shining example of the kind of superb graduate student that we are lucky enough to have at this university, and that you can see here today. Jackie joined my lab to study nuclear pore complexes, the massive machines that act as the gatekeepers of the cell's nucleus. Jackie chose to study how proteins called FG nups work; these are the proteins in the nuclear pore complex that actually mediate transport of materials into and out of the nucleus.

At the time, I think no one, least of all me, appreciated quite how much of a challenge this project was going to be. We began to realize why so few people have published anything on FG nups. It turns out that these are incredibly difficult proteins to make and to work with, and had I known I definitely wouldn't have wished them on such a nice person as Jackie.

However, Jackie's mild nature disguises an extraordinary level of bubbly enthusiasm, intelligence, dedication and determination to solve problems. She clearly believes in the proverb that you cannot get to the top by sitting on your bottom. Because of this, she developed methods to purify perhaps 1,000 times more of the FG nups than anyone else had previously made, systematically solving problems of the kind that would have made most people give up. But giving up doesn't come easily to Jackie!

This has allowed her, for the first time, to develop and apply numerous cutting-edge assays that have revealed surprising new aspects of the way these peculiar proteins work. This includes learning how FG nups can stop the wrong materials crossing the nuclear pore complex while letting the right things get through, and helping to build the first artificial nuclear pore complex.

Jackie has also proved to be a fantastic colleague in the laboratory, always happy to offer a helping hand. She has contributed tremendously to the life of the laboratory and has made sure she's enjoyed life in general in New York. She is usually a key organizer of our lab parties, is a keen cello player, and I understand she's seen just about every Broadway musical playing.

I'm really happy to see Jackie graduating today, launching her into what is sure to be a sparklingly successful future. Jackie's work continues to spawn new lines of research, and Jackie herself is carrying on her FG nup work, so we're lucky that she'll be around being the life and soul of the lab for a little longer!

Christopher Tinkle* presented by Elaine Fuchs

B.A., The University of Texas, Austin

Dissecting the Functions of Classical Cadherins in Skin

Chris Tinkle received his B.A. in microbiology from The University of Texas, Austin. He gravitated toward cancer biology at the University of California, San Francisco, where he served as a research technician studying cancer and inflammation. Chris contributed to the major discovery that although mutant oncogenic cells drive the development of cancer, the healthy inflammatory cells that enter the microenvironment to kill the cancer cells can express key factors that influence tumor progression and metastasis.

When Chris entered the MSTP program here, I was fortunate that squamous cell carcinomas of the skin served as the tumor model in his UCSF studies that had sparked Chris's passion for biomedical research.

In my laboratory, Chris's rotation project formed the backbone of his thesis project, and he published within his first full year in the lab. Chris tackled the problem of why loss of an intercellular junction protein, E-cadherin, is frequently associated with human cancers and yet in the lactating mammary gland, its loss results in tissue dysfunction and cell death. He uncovered a backup system that epidermal skin cells use to counteract the loss of E-cadherin and survive, and showed that those tissues such as hair cells of the body lack the backup and die. Importantly, Chris discovered that skin

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Coming soon, to The David Rockefeller Graduate Program

Plans for Convocation kept many offices busy this spring, but behind the scenes, another group was already planning for the fall. Rockefeller's application screening committee pored over 675 applications of potential new students, eventually winnowing the list down to 67 acceptances. Of those, 22 have enrolled to begin The David Rockefeller Graduate Program this fall.

The new class includes 13 men and nine women from nine countries: Argentina, Bulgaria, China, Columbia, Romania, Singapore, Slovenia, the United Kingdom and the United States. Their alma maters include: Berlin University of the Arts, Charité Berlin Medical School, Harvard University, Howard University, Kenyon College, Michigan State University, Oberlin College, Peking University, Princeton University, Rutgers University, Smith College, The State University of New York, Binghamton, Tufts University, University of Buenos Aires, University of the Andes, University of Bristol, University of California, Santa Barbara, University of Ljubljana, University of North Carolina, Chapel Hill, Wesleyan University and Yale University.

hyperplasia, a precancerous state, develops in these mice with age, suggesting that the backup system is not a perfect one. He went on to delve deeper into these mechanisms and published a second paper, highlighted in the *Proceedings of the National Academy of Sciences* this past year. Chris's findings, first at UCSF and now at Rockefeller, have helped researchers to understand cancer progression and metastasis, and in the future will be useful in developing new and improved methods for tumor therapy.

On a personal note, Chris was a soft-spoken giant in the laboratory, serving as the most rigorous critic of his own research. However, Chris also coupled this seriousness to a good sense of humor and an ability to let his hair down at the right moments. He'll make a wonderful physician-scientist with a genuine dedication to cancer biology.

Kelly-Anne Twist presented by Seth A. Darst

B.Sc., B.Sc. Hon., Victoria University of Wellington

Structural Studies of Three Factors That Affect the Prokaryotic Transcription Cycle: Microcin J25, Lambda Q and T4 GP33

I have the pleasure of introducing you to Kelly-Anne Twist. I think Kelly-Anne would consider herself a native New Zealander, but she also spent some of her formative years living on the island of Niue.

Kelly-Anne came to the lab with a strong desire to learn a technique called x-ray crystallography and began working on a collaborative project to synthesize and characterize a peptide inhibitor of RNA polymerase. We thought this would take a few weeks and could ultimately lead to a crystal structure of the complex with RNA polymerase. This turned out to be the beginning of an amazing adventure, with Kelly-Anne at the center of it, to determine the structure of this inhibitor. In the process, Kelly-Anne learned peptide chemistry, biochemistry, advanced mass spectrometry techniques, as well as NMR, but the work did not lead to any x-ray crystallography.

Kelly-Anne then set out on a number of other projects with the goal of using x-ray crystallography to determine structures of transcriptional regulatory proteins. Kelly-Anne made a number of contributions, but none of these projects led to a crystal structure either.

As many crystallographers will readily admit, success at crystallography involves a pinch of luck, and finally Kelly-Anne got lucky. She crystallized and determined the structure of an interesting complex involved in transcription regulation by T4 phage.

During all this, Kelly-Anne has been successfully engaged in another collaborative project, where she's working with her husband Malcolm to raise their lovely daughter, Leona. I wish Kelly-Anne and her family continued luck.

Marc Paul Waase* presented by Jan L. Breslow

B.S., Cornell University

The in Vivo Characterizations of Two Novel Genes in Mus musculus*:* ADAM11 *and* StARD5

It has been my privilege to work with Marc Waase since the summer of 2004, when he did a rotation in my laboratory followed by his Ph.D. thesis work. Marc came to my laboratory quite prepared. As a high school student, he participated in the Rockefeller/Cornell/Sloan-Kettering Gateways Program, where he worked for two summers in the laboratory of then-Rockefeller University professor Markus Stoffel. As an undergraduate at Cornell, Marc did extensive research on the genetics of DNA mismatch repair in yeast, while majoring in biological sciences.

Marc's Ph.D. thesis work entailed characterizing the functions of two novel cholesterol regulated genes: *StARD5* and *ADAM11*.

StARD5 is a member of the START family of proteins, which contain an approximately-200-amino-acid motif forming a hydrophobic pocket that binds and transports intracellular lipid, in this case cholesterol. StARD5 is made in macrophages and is up-regulated by free cholesterol loading as part of the ER stress response. *ADAM11* is a disintegrin and metalloproteinase family member that is up-regulated in the livers of mice fed cholesterol. Marc made mouse knockout models for both of these genes. In spite of our expectations and Marc's meticulous experiments, these mice had no phenotype with regard to altered plasma, liver or biliary lipids. Even when Marc bred his knockouts onto the atherosclerosis-prone ApoE knockout background, there was no effect on lesions. In spite of these negative results and as a true test of character, throughout, Marc maintained a great constructive attitude, worked indefatigably and was a wonderful citizen of our laboratory. Toward the end of his thesis work, Marc's persistence paid off and he was able to show unexpected phenotypes for both knockouts. Homozygous *StARD5* knockouts died prior to embryonic day seven, indicating a role in early embryogenesis, and homozygous *ADAM11* knockout mice developed petit mal epilepsy.

Marc's parents have been very supportive of his career, and his sister Karine provided Marc an excellent role model, having preceded him in the M.D.-Ph.D. program by a few years. During his thesis work Marc took time out to marry Cecelia, whom he had met when they were both undergraduates at Cornell. Marc has all of the ingredients to be a very successful physician-scientist and I wish him every success in his future career.

Homare Yamahachi presented by Charles D. Gilbert

Licenciado, University of Buenos Aires

Circuit Dynamics of Adult Visual Cortex

Homare (Matias) Yamahachi did his undergraduate degree in biology at the faculty of natural sciences, University of Buenos Aires, Argentina. His work involves making a window on the living brain to look for changes in brain circuitry that are associated with sensory experience and learning. His studies combined fluorescent labeling of neurons and their connections by gene transfer with viral vectors. This technique was combined with high-resolution two-photon imaging, which allowed him to image individual synapses, all in the intact, living brain. While the study of cortical circuitry had previously been done with postmortem anatomical tools, these tools did not allow one to see the circuit dynamics. Using high-resolution in vivo imaging, Matias, along with his collaborators, found that the circuits of the visual cortex are highly dynamic, turning over synapses at a rate of seven percent per week. And these changes occurred in the adult brain. Extending these studies to a model where he altered sensory experience, he found even more dramatic changes in cortical circuits, with very rapid alterations in circuitry involving an exuberant effluorescence of new connections paralleled by a pruning of old connections. These results led to a new view of brain circuitry. While the old view held that the connections in the brain are fixed after a critical period early in postnatal life, these results point to an ongoing process of sculpting cortical circuits, with new connections being formed and old connections being eliminated.

Matias's interests lie at the interface of technology and biology, and going forward he would like to continue engineering new experimental approaches, while applying them to important biological problems.

Yun Zhong presented by Nathaniel Heintz

B.E., M.Eng., Osaka University

Biochemical and Genetic Studies of Beclin 1 Function in Autophagy

Yun Zhong arrived at Rockefeller from Osaka University, having completed both bachelor's and master's degrees in biophysical engineering. While at Osaka, Yun won a series of prestigious student awards, including a Japanese Government Scholarship that is awarded to only one student at Osaka University each year. Upon arriving at my laboratory, Yun expressed a strong interest in neurodegeneration, fueled by a recent paper from my lab demonstrating that the process of autophagy is induced during degeneration of a very particular neuron type, the cerebellar Purkinje cell, in a mouse model of ataxia. Autophagy, as the name suggests, is a tightly controlled catabolic process in which the cell recycles its constituents to provide nutrients for essential metabolic processes under conditions of stress. The cell literally eats itself. Of course, as we all know, too much eating can be a very dangerous thing; consequently, autophagy is very highly regulated in all organisms. Although pioneering work from several laboratories had defined a conserved pathway consisting of approximately 40 proteins that execute this program in yeast and invertebrates, the mechanisms controlling this pathway in the mammalian brain were largely unexplored. It is this topic that formed the basis for Yun's doctoral studies.

Given our commitment to exploring the details of this pathway in the context of neurodegeneration in the mammalian brain, Yun chose to join forces with the laboratories of Zhenyu Yue and Brian Chait to identify the components of a protein complex regulating the induction of this pathway in the brain. Through a combination of mouse molecular genetics, biochemistry and mass spectroscopy, Yun and his colleagues were able to identify two new components of this very important pathway and demonstrate that they orchestrate its induction in neurons and other cells. Yun has gone on to show that this complex is also essential for maintenance of the complex membrane trafficking events that are so crucial for the function of this large and complex brain cell type.

Yun is a man of few words. Our conversations are brief and to the point. To tell you the truth, this worried me for a while. After all, all of us like to feel that we are important in the scientific pursuits of our young colleagues! But I soon realized that Yun speaks with his hands: The experiments he conducts and the astounding clarity of his results communicate his intelligence, creativity and impressive experimental facility much more effectively than the spoken or written word! In this way, Yun reminded me again that it is the well-done experiment that is the currency of our profession. Seeing his results unfold was a real pleasure, instilling in me the confidence that this young man would make important contributions to science, whether or not he heeded my advice.