7-2013

BenchMarks 2013, July 26

The Rockefeller University

SCIENCE FOR THE BENEFIT OF HUMANITY

BENCHMARKS

THE COMMUNITY NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

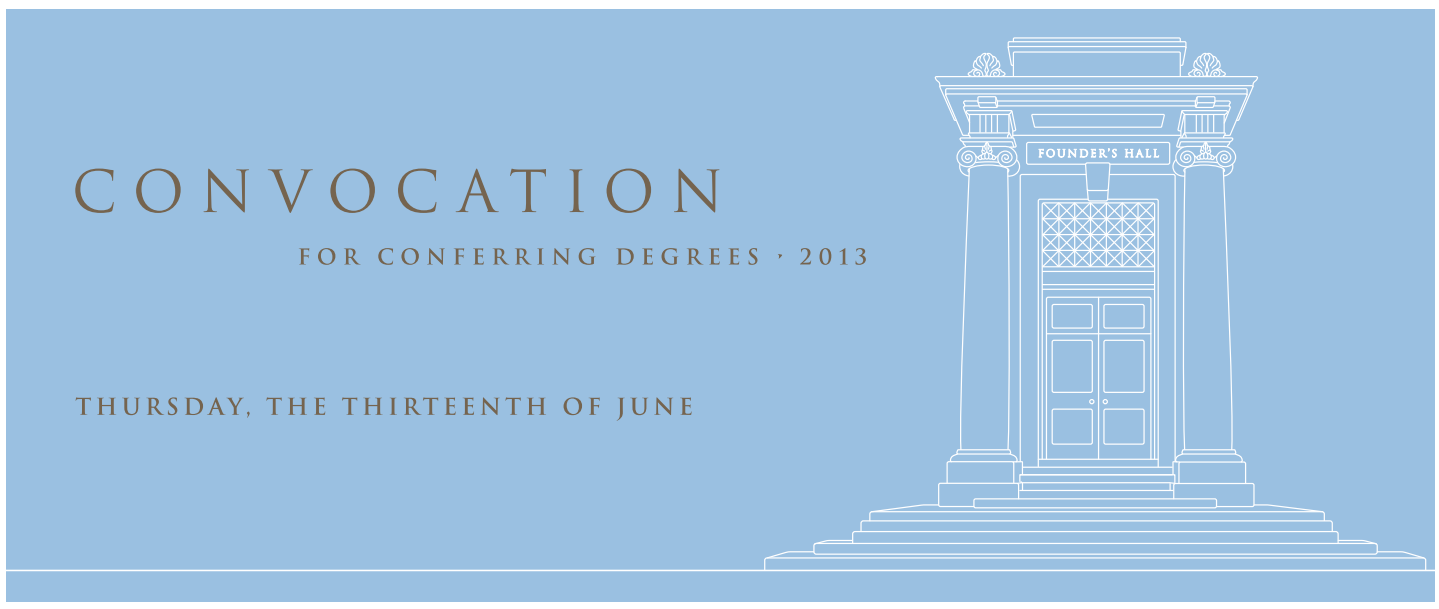
FRIDAY, JULY 26, 2013

The 2013 Convocation awarded 17 Ph.Ds to Rockefeller graduate fellows, bringing the total number of Rockefeller alumni to 1,127. Although rain in the early afternoon forced the cancellation of the traditional academic procession from Weiss to Caspary Auditorium, it did not dampen spirits. Following tradition, faculty mentors presented each student at a formal ceremony in Caspary. Afterwards, the campus community turned out for a reception in Weiss Café to celebrate the graduates.

Members of the class of 2013 — seven men and 10 women — come from six countries: Argentina, India, Italy, Malaysia, Turkey and the United States. They have secured or are interviewing for positions as postdoctoral fellows and consultants, as well as roles within the biopharmaceutical industry. Participants in the Tri-Institutional M.D.-Ph.D. Program will return to medical school to finish their medical degrees.

This annual Convocation issue of BenchMarks *salutes the university's class of 2013.*

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



PHOTOS: SCOTT RUDD PHOTOGRAPHY AND ZACH VEILLEUX.

BENCHMARKS

Marc Tessier-Lavigne, President
Jane Rendall, Corporate Secretary

Zach Veilleux, Executive Editor
Leslie Church, Assistant Editor

BenchMarks is published monthly and is distributed on the campus of The Rockefeller University. It is produced by the Office of Communications and Public Affairs. The Rockefeller University is an affirmative action/equal employment opportunity employer.

Printed with vegetable-based inks on recycled paper made from 100% postconsumer waste.

David Rockefeller Fellowship awarded to neuroscientist Jason Pitts

by LESLIE CHURCH

Jason Pitts wasn't entirely sure what to do with his life after graduating from college, back in 2008. So like any good scientist facing a big question, he came up with a series of experiments. Mr. Pitts tested out several careers — from medicine to teaching to pharmaceuticals — before concluding that bench science was his true passion and grad school was where he belonged. Mr. Pitts, now a graduate fellow in President Marc Tessier-Lavigne's lab, was recently honored for his dedication to thoughtful research and community service at this year's Convocation luncheon, where he was awarded the David Rockefeller Fellowship.

PHOTO: SCOTT RUDD PHOTOGRAPHY

A fine fellow. Jason Pitts was awarded the David Rockefeller Fellowship at the Convocation awards luncheon, for showing outstanding promise in science and leadership. Mr. Pitts is a graduate fellow in the Tessier-Lavigne lab, where he studies axon degeneration. He is also president of the Tri-Institutional Consulting Club, which holds talks on scientific careers outside of academia.

The fellowship is given annually to a third-year student who shows outstanding potential in science and leadership, and Mr. Pitts, who studies the molecular mechanisms of axon degeneration, has carved out a career path that includes an ample amount of both.

A native New Yorker from Suffolk County's south shore, Mr. Pitts studied biology at Cornell University. Then, through Teach for America, he spent a year as a science teacher in Hartford, Connecticut, where he taught general science to seventh and eighth grade students. During that time, he shadowed doctors at a nearby hospital in Providence while considering medical school. Mr. Pitts then joined Regeneron Pharmaceuticals in Tarrytown, New York, as a research associate in a bi-specific antibody group. It was there that he realized his passion for bench science, and a colleague at the company suggested Rockefeller.

"I am a big fan of independence, and the fact that Rockefeller not only allows you, but encourages you to pick your own path and mold your own education was a big draw for me," says Mr. Pitts, who came to the university in 2010. "Of course, even with those great features, the thing that really drew me to Rockefeller was the chance to work with world class faculty."

After a few lab rotations, Mr. Pitts found he felt right at home in Dr. Tessier-Lavigne's newly established Laboratory of Brain Development and Repair. He was able to build on the work of a previous lab member looking at how the body decides which axons to keep and which to prune back as the nervous system is sculpted during development.

"There is still so much that is unknown about this process and the chance to discover something that could not only prove fundamental to development but also might lead to future therapies in diseases like ALS and Alzheimer's is immensely encouraging to me," says Mr. Pitts.

"Jason's scholarship is evident both in the manner in which he has guided the direction of his project as well as in his scientific accomplishments," says Dr. Tessier-Lavigne, Carson Family Professor at Rockefeller. "He is a creative and thoughtful scientist and I am confident that this award will be just one of many honors in his career."

Outside of the lab, Mr. Pitts volunteers as a mentor in the Rockefeller Summer Neuroscience Program, which introduces area high school students to methods in brain research and guides them through experiments in their own small study. He is also president of the Tri-Institutional Consulting Club, which gives students a look at careers outside of academia. The topic is of special interest to Mr. Pitts as he looks toward life after graduation.

"I enjoy bench science, but I am also very interested in applying the scientific skills I've acquired here to other areas. I think there is a big need for scientists to get out of labs and engage with other disciplines, so I could also see myself working on public policy or consulting," he says.

Coming soon, to The David Rockefeller Graduate Program

As the graduating class of 2013 moves on to the next stages of life and career, the Rockefeller community welcomes the incoming group of graduate fellows. There were 719 applications received this year, and after careful consideration by the admissions committee, 69 applicants were offered admission to the university. Twenty-four students will enroll — 13 men and 11 women from 6 countries: China, Japan, Korea, Spain, Turkey and the United States. Their alma maters include: Ankara University, Autonomous University of Madrid, Bogazici University, Brown University, Columbia University, Cornell University, Johns Hopkins University, Korea Advanced Institute of Science and Technology, Massachusetts Institute of Technology, Northwestern College, Peking University, Reed College, Rhodes College, Stony Brook University, the University of Chicago, University of Georgia, University of Notre Dame, University of Pennsylvania, University of Pittsburgh, University of Rochester and University of Tokyo.

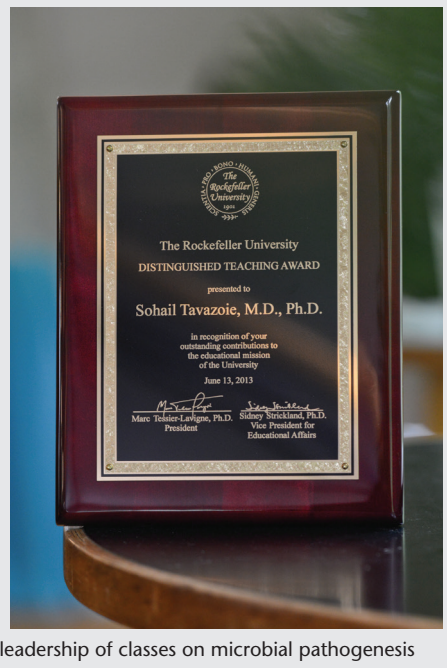
Marraffini and Tavazoie recognized for excellence in teaching

Two Rockefeller faculty members were honored at the Convocation luncheon with this year's Distinguished Teaching Awards: Assistant Professor Luciano Marraffini and Leon Hess Assistant Professor Sohail Tavazoie. It is the 10th year that the awards, which recognize excellence in and dedication to the university's educational environment, have been given to Rockefeller faculty members. Dr. Marraffini, head of the Laboratory of Bacteriology, and Dr. Tavazoie, head of the Elizabeth and Vincent Meyer Laboratory of Systems Cancer Biology, were recognized for their passion and commitment to education at Rockefeller.

Dr. Marraffini assumed a leadership role in 2012 for the successful Microbial Pathogenesis course, which entails a three-hour lecture and discussion focusing on the molecular mechanisms of host-pathogen interactions and pathogenesis of representative bacterial, fungal and protozoan diseases. The course brings Rockefeller and Cornell faculty and guest speakers to the classroom. Dr. Marraffini is now organizing the 2014 course.

Dr. Tavazoie was co-organizer of the Molecular Basis of Cancer course with Titia de Lange in 2009, a course which he then took over in 2011 and 2013. The course is designed to teach modern concepts in the regulation of growth control and its significance to cancer. The format consists of a weekly, two-hour lecture followed by informal discussion over lunch.

"Requirements are rigorous for these courses, in terms of what is asked of students and what is asked of the teacher," says Marc Tessier-Lavigne, Rockefeller's president. "Luciano and Sohail are recognized for their commitment to the education of young Rockefeller scientists, in the laboratory and in the classroom."



PHOTOS: SCOTT RUDD PHOTOGRAPHY

Classroom competence. Luciano Marraffini (top) and Sohail Tavazoie received teaching awards for their leadership of classes on microbial pathogenesis and the molecular biology of cancer, respectively. The awards were presented at the Convocation luncheon.

Four leaders in science and philanthropy given honorary degrees

by LESLIE CHURCH

At this year's Convocation ceremony, honorary degrees were awarded to four proponents of basic science who have made invaluable contributions to science, through research and philanthropy. Günter Blobel, John D. Rockefeller Jr. Professor at Rockefeller; Paul Greengard, Vincent Astor Professor at Rockefeller; and James and Marilyn Simons, leaders in the philanthropic community, each accepted degrees.

Dr. Blobel, who started his career at Rockefeller as a postdoc in 1967, is considered a major figure in cell biology. He received the 1999 Nobel Prize in Physiology or Medicine for his research on protein transport, which revealed the existence of a cellular "zip code" system that provides newly made protein molecules with highly specific addresses, guiding them to the part of the cell to which they are assigned. Dr. Blobel answered a crucial question of cell biology that had loomed over the field for decades, and in turn he expanded scientific understanding of several inherited diseases.

Dr. Blobel is originally from Waltersdorf, Germany, now a part of Poland, and attended the University of Tübingen, receiving his M.D. in 1960. He earned his Ph.D. in 1967 from the University of Wisconsin, Madison. When Dr. Blobel was a child, his family fled the advancing Red Army of the Second World War, and found themselves near Dresden, a cultural center that was soon after fire-bombed by the allied forces. The event made a significant mark in the scientist's memory, and decades later he became the founding president of Friends of Dresden, an organization that has played a major role in reconstructing and restoring historic buildings in the city. He donated his entire Nobel monetary winnings toward the reconstruction of a landmark church and the construction of a new synagogue. At the ceremony, Dr. Blobel had a few words of wisdom for the graduating class.

"Keep a child's curiosity," he said. "Learn through teaching. If your grandmother doesn't understand what you are doing, you probably don't understand either. Invite criticisms, and accept opposition to your ideas, but trust your instincts and stay the course."

Dr. Greengard is also respected as a pioneer in his field — that of neurobiology. In the 1960s, when most neuroscientists were concentrating almost exclusively on the role of electrical impulses in the brain, Dr. Greengard chose to focus on the brain's chemistry instead. He was honored for his transformative work in 2000, when he shared the Nobel Prize in Physiology or Medicine for his discovery of how dopamine and a number of other neurotransmitters exert their action in the nervous system, work that has led to new insights in treatments for Parkinson's disease, schizophrenia, depression and attention deficit/hyperactivity disorder.

Dr. Greengard earned his Ph.D. from Johns Hopkins University, where he helped establish a new department of biophysics with Detlev Bronk, who would later become president of Rockefeller. His academic career took him from the University of London to Cambridge University, the University of Amsterdam, the National Institutes of Health and Yale University. Dr. Greengard joined the faculty at Rockefeller in 1983, and since 1994, he has also headed the university's Fisher Center for Alzheimer's Disease Research. Together with his wife, the sculptor Ursula von Rydingsvard, Dr. Greengard donated his Nobel winnings to establish the Pearl Meister Greengard Prize. Named in honor of his mother, who died giving birth to him, the annual international award recognizes the accomplishments of women in science.

Marilyn and James Simons were honored for their dedication to encouraging high-risk, high-reward research.

"What sets Jim and Marilyn apart from many benefactors is their deeply held belief in the importance of basic research," Marc Tessier-Lavigne, Rockefeller's president, said at the ceremony. "They understand that basic science requires patience, but that in the long run — and sometimes in the short term — it pays huge dividends. Theirs has been 'institution building' philanthropy, and all of us in this great hall today have benefitted from their vision and largess."

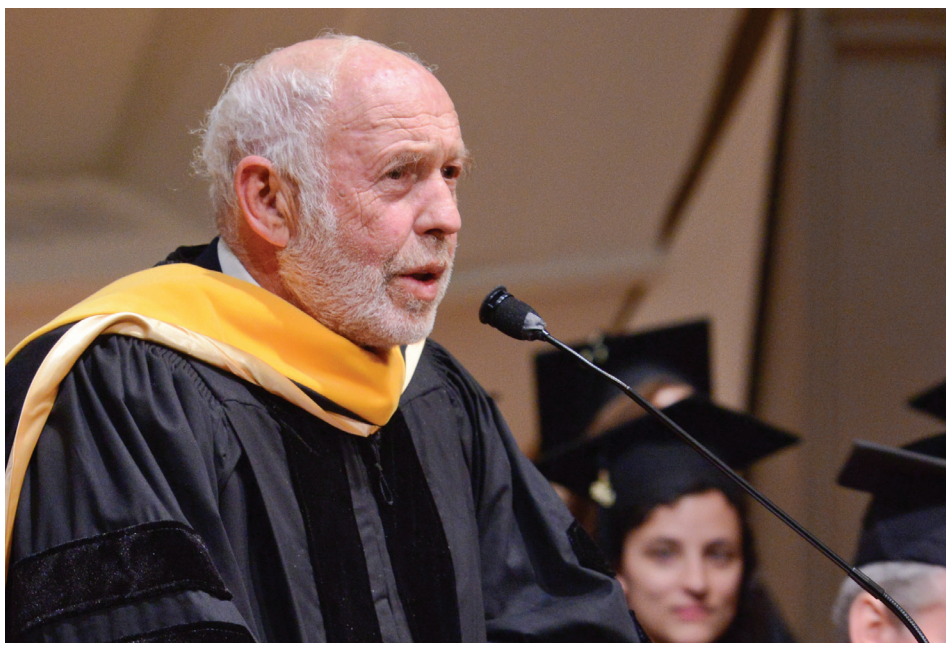
James Simons began his career in academia. He earned his Ph.D. in math from the University of California, Berkeley, at age 23. He subsequently taught math at the Massachusetts Institute of Technology and Harvard before becoming a cryptanalyst for a U.S. Department of Defense think tank at Princeton University, breaking military codes during the Vietnam War. He then made his way to the State University of New York at Stony Brook, where he served as chair of the mathematics department, building it into one of the world's top centers for geometry and earning accolades for his own work in differential geometry. In the late 1970s, Dr. Simons left academia for finance, starting Renaissance Technologies, which pioneered the use of quantitative analysis to make investment decisions and quickly became one of the top performing investment firms in the world.

Dr. Simons's commitment to math and science education can be seen through his many philanthropic roles — in addition to being a Rockefeller trustee, he created the Math for America program, whose mission is to improve science, technology, engineering and mathematics education in U.S. public schools. He is chairman of the Simons Foundation, the charitable organization that his wife leads, and serves on the boards of many other prestigious institutions, including the Institute for Advanced Study, MIT and Brookhaven National Laboratory. At the ceremony, Dr. Simons discussed his appreciation for the role of mathematics in biology.

"[I've been] gratified to see that mathematics has found its way into many aspects of life science," Dr. Simons said. "The sophistication of the mathematics being applied to biology has increased. But even if … mathematics is never a full partner in life science as it is in physical science, it will surely come to be its indispensable loyal servant. It behooves all of you setting out on this quest to arm yourselves for the journey by learning as much mathematics as you possibly can."

Marilyn Simons is noted for her role as president of the Simons Foundation and is considered to be one of the leading advocates in the United States for research on autism. The Simons Foundation, created in 1994, is a major funder of basic scientific research, in areas including mathematics, physics, life sciences and autism. Through the foundation's encouragement, many of the world's prominent geneticists, biologists and clinicians have chosen to include the search for the cause of autism in their research. Simons Science News, a division of the foundation, aims to enhance public knowledge of science and math by providing editorially-independent, lay-friendly research news online. Dr. Simons, who earned her Ph.D. in economics from the State University of New York at Stony Brook, is also active with several programs dedicated to educating children, particularly those with special needs. She is a past president of the board of the LearningSpring School, a private New York City school for children on the autism spectrum, and at Rockefeller, she is an active member of the *Women & Science* initiative.

"Politicians and special interest groups influence many decisions critical to our country. We need the voice of scientists," Dr. Simons said to the graduates. "Many of you will use your education and imagination to excel in research. I'd like to suggest that you also use your talent to share your discoveries and your passion with others. … Your sense of wonder and vision give us hope for a better world tomorrow, and sharing that is the most compelling message of all."



PHOTOS: SCOTT RUDD PHOTOGRAPHY

Degrees of honor. The four honorary degree recipients at this year's Convocation ceremony in Caspary Hall have made their mark in basic science, through research and philanthropy. Clockwise from top left: Günter Blobel, Paul Greengard, James Simons and Marilyn Simons.

The 2013 Graduates

Following tradition, faculty mentors gave congratulatory tributes to this year's graduates. These are the transcripts of those speeches, as they were delivered on June 13. Students in the Tri-Institutional M.D.-Ph.D. Program are denoted with an asterisk. Three students graduated in absentia: Ryan W. King, María Maldonado and Nirmala Ramalingam.

Pinar Ayata

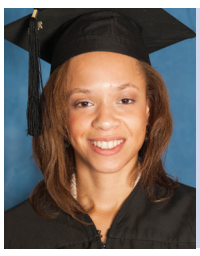
presented by Nathaniel Heintz

B.S., Sabanci University
Decoding 5hmC as an Active Chromatin Mark in the Brain and its Link to Rett Syndrome

As I stand here before you, I feel a real sense of pride in Pinar Ayata's achievements. This young woman has so many facets to her personality, and such strong passions for nature and the world about us, that I at first thought that she would have difficulty finding the balance between science and society that we all must achieve if we are to survive in this field of endeavor. My concern was entirely unnecessary. Pinar has been blessed with the boundless energy and enthusiasm to embrace life each day as a new experience, a deep intelligence to guide her with clarity toward her scientific goals and an unfailing optimism that carries her through the storms of the scientific research experience. These qualities have allowed her to make startling discoveries in the field of epigenetics and Rett syndrome, while at the same time scouring the world for more remote mountains to climb, snow fields to traverse and rivers to kayak. Rockefeller has served Pinar very well: she has developed a talent for life and science that eludes many of us for decades.

In 2009, my laboratory discovered that mammalian genomes contain a sixth nucleotide, 5hmC, which is particularly abundant in the brain. This ignited a fire in epigenetics research that continues unabated today, leading to publication of over 250 original research articles in these few years. Yet as interesting as these many papers have been, it is Pinar's discovery of the mechanism for decoding 5hmC in the nervous system that has shed the most light on this new process for genome regulation. Through a series of beautifully executed biochemical experiments, Pinar discovered and proved definitively that the protein that reads this new mark in the genome is encoded by the gene that is causative for Rett syndrome — a devastating autism spectrum disorder that afflicts young girls. I found this result shocking because the Rett syndrome protein had been discovered decades earlier, and two major laboratories had reported that it cannot bind 5hmC — so I bet Pinar that something must be amiss, that there has to be another protein interpreting this new genomic signal in the brain. With the exacting experimental skill that is typical of Pinar, she proved me wrong, publishing her results in a landmark *Cell* paper and winning a bottle of champagne (which I have yet to pay her).

As I hope you can appreciate from these comments, Pinar's childhood in Istanbul, her early experiences sailing the Turkish coast with family and friends, her educational experiences at Sabanci University and her scientific internships in Heidelberg and Boston seem to have primed her for scientific and personal explorations that stretch the imagination. I have been fortunate to watch as these excursions into the unknown bore fruit, and I am confident that they will continue to do so during her postdoctoral studies in the laboratory of Anne Schaefer at Mount Sinai School of Medicine.



Nicole Bowles

presented by Bruce S. McEwen

B.A., New York University
Cannabinoid CB_1R Receptor Mediates Metabolic Syndrome in Models of Circadian and Glucocorticoid Dysregulation

Nicole Bowles graduated from New York University in May 2008 with a B.S. in chemistry and minor in math.

Prior to coming to Rockefeller, Nicole had worked as a summer researcher at the University of Pennsylvania and then the Joslin Diabetes Center, and the next year at Merck Pharmaceuticals, and finally, after graduating from NYU, at the Mount Sinai department of pharmacology, studying endocannabinoids.

Endocannabinoids are the body's own chemicals that are the reason it responds to marijuana, and they are increasingly recognized as having many important functions in the brain and throughout the body. (A parallel example: endogenous opioids are the reason the body responds to painkilling and addictive opioids.) Matt Hill and Ilia Karatsoreos were postdoctoral members of my lab at the time she joined it with interests in endocannabinoids and circadian clocks, respectively, as part of our ongoing work on stress effects on the brain and body. Nicole officially joined our laboratory in spring of 2009. Along with her past work and interests and advice from Matt and Ilia, this led to her thesis, titled *Cannabinoid CB_1R Receptor Mediates Metabolic Syndrome in Models of Circadian and Glucocorticoid Dysregulation*.

So what did Nicole find?

Our stress hormones and the body's own biological clocks play a key role in metabolism and regulation of body weight, and Nicole's thesis addressed how the stress hormone cortisol and disruption of the normal daily biological rhythm regulated by those clocks contribute to obesity and metabolic syndrome. Nicole discovered that mice lacking the cannabinoid CB_1 receptor were protected against all of these changes in metabolic function. Moreover, blocking the CB_1 receptor, not only globally, but also through targeted peripheral inhibition, suggested that the endocannabinoid system mediates glucocorticoid induced metabolic syndrome not in the brain, but in the body itself.

In addition to her ambitious and successful laboratory work for her Ph.D. thesis that Nicole managed with great efficiency, she volunteers in a diverse array of community activities, in the United States and abroad, that are directed to helping overcome the effects of poverty, social inequality and discrimination.

Upon coming to Rockefeller, Nicole joined and soon became the cochair of our campus Student Pugwash, which examines the relationships between science and society and the common goal of ensuring that scientific research benefits humanity.

She has also applied this interest directly by volunteering to help individuals and families in her own neighborhoods of Philadelphia and New York, for example, through Meals on Wheels and events sponsored by New York Cares, including weekly tutoring at a public high school and preparation work for soup kitchens. And she has also used winter and spring breaks for Habitat for Humanity week-long construction projects in Virginia and North Carolina, along with a trip to New Orleans for the continual hurricane relief efforts. She used her two week vacation time in 2011 to travel to Peru and work on childhood education. Clearly Nicole is not only an excellent scientist but has an incredible social conscience and puts this into practice. Her next steps will be to continue in our laboratory as a postdoctoral fellow while pursuing a Master's degree in epidemiology and public health across 68th Street at Weill Cornell Medical College.

Fabio Casadio

presented by C. David Allis

B.S., M.S., University of Bologna
Discovery and Characterization of Methylation of Arginine 42 on Histone H3: A Novel Histone Modification with Positive Transcriptional Effects

Fabio Casadio came to my lab from Italy, which is relevant, but he came carrying an interest in what turned out to be the centerpiece of his work in my lab, a topic called arginine methylation. I say that Italy is relevant because I'd like to welcome his parents, who are here from Italy, and certainly proud of him, and we are as well.

Back to arginine methylation, I'll keep it simple. I'll just say that in the current views of our day this is the little brother of a big brother, lysine methylation, which seems to be guiding our genome and in fact watching out for the arginine methylation below it. That makes it very rare, and it makes it very challenging, but Fabio in fact cracked that open and taught us quite a bit about this little brother. He taught us who puts this mark on, who takes this mark off, and most importantly, how it functions in the cell.

Fabio mapped the site, in terms of the structure that we study in the lab, which is so critically positioned to be a genetic switch that might open or close our genetic material. Fabio put forward the hypothesis that may indeed be what this modification was all about, and went on to test this in a defined chromatin system that took advantage of work with Bob Roeder and Tom Muir.

Relevant on a personal level, Fabio wasn't just smart and quick upstairs; he was actually quick downstairs, meaning his feet. Fabio is a very big sports man, and in fact, of the many sports that he did while he was here, he regularly entered all the premiere marathons. But maybe more surprising to me was that he came in as an elite marathon top-tier runner in all of those races. I know a lot of Rockefeller students dominate, but Fabio is even a notch above.

So what's he going to do with all this stamina and discipline? He's decided to take another course: he's going to take his smarts and quick wits to McKinsey & Company, and we know that he's got all of the background ingredients for this because he can be so disciplined and has the stamina and the strength. But in fact I learned recently, when Fabio graduated, that he has been turned on to one American delicacy. This is a calorie packed food; it's cheap and that makes it graduate student friendly. And it turns out to be nothing other than peanut butter. Fabio loves peanut butter. I actually have an added present for Fabio's parents. I've already gotten Fabio a big jar of peanut butter but I'd like him to take this Reese's back to his parents because they've traveled so far; this may help them on the return trip.

Emily Conn Gantman

presented by Robert B. Darnell

B.A., University of Pennsylvania
RNA Dynamics in T Cell Activation

Emily Conn Gantman came to The Rockefeller University as an extraordinarily promising young talent and emerged an outstanding multi-disciplined scientist, humanist and . . . a mother. A lot to get done during the course of a Ph.D.

Emily came to Rockefeller very accomplished from the University of Pennsylvania with a 3.9 GPA and wide range of research experience. This included clinical research at the Children's Hospital of Philadelphia and basic science in *Arabidopsis*, work that earned her the Rose Undergraduate Research Award at Penn. She was a true scholar, presaging her time at Rockefeller with A pluses in her last year in a range of courses including computational biology and physics (although I have to admit she did not approach physics in our lab). She followed Penn with a one year fellowship at the NIH on developmental biology, striking the balance between clinical and basic research that would again presage her graduate work.

She came to Rockefeller interested in molecular mechanisms of disease, and carried her erudition over to the university, earning honors in coursework here, something I didn't know we even handed out. Even my father, known to be a bit reserved in giving compliments, called her term paper "imaginative." Her interests were a natural fit for our lab, and she began a series of extremely ambitious and imaginative proposals, earning her a *Women & Science* fellowship from the university. The range of work she accomplished is breathtaking … it's almost embarrassing to me as I look over it, to think that I would let someone be so broad in their approach to the lab. But Emily was unstoppable. She was the first and to date only graduate student to fully embrace both sides of my lab, the more clinical side (what we affectionately call the "West Coast lab") and the basic side (the "East Coast," nothing to do with California versus New York). She developed really two theses in one, falling in love with questions of what drives anti-tumor immunity in patients with rare disorders — paraneoplastic neurologic disease — in which they can eradicate their cancers, even while being attracted to more basic questions of mechanisms underlying the activation of T cells.

It was the latter work that ended up consuming the bulk of Emily's efforts. She had an amazing ability to project her own limitless enthusiasm and delight for science onto others, which ended up first intellectually engaging them, then charming them into working collaboratively with her. This led to an extraordinarily complex thesis, genuinely going where no one has gone before, to look at detailed aspects of regulation of the "dark matter" of the genome — the regulation of RNA, both by RNA binding proteins and other, microRNAs, in resting and in activated T cells. Her work will, I truly believe, be recognized as a foundational study in the years ahead.

Emily's ability to gather support from colleagues turned out to be especially useful after

she gave a special lab meeting one day. At the end of an hour of detailed data, she showed a fuzzy black and white picture that turned out to be an ultrasound showing a little tiny girl in her uterus! This turned out to be a wonderful means of aggregating help, as no one would let her within 10 meters of any isotope, and she in fact ended up redoubling her collaborations in the group. She is now a happy mother, and looking forward to coming back to the lab for a year's postdoc as she plans her future as a woman in science.

Teresa Davoli

presented by Sidney Strickland on behalf of Titia de Lange

B.S., University of Pisa
M.S., San Raffaele University
Telomere-driven Tetraploidy and its Relevance to Cancer

I will read remarks prepared by Titia de Lange who unfortunately couldn't be here today:

It is difficult to do justice to Teresa Davoli's remarkable talent in the two minutes allotted to each graduating student. Teresa left campus about a year ago to join Steve Elledge's lab at Harvard University, where she is supported by a Helen Hay Whitney Fellowship. Here at Rockefeller she was honored with the David Rockefeller fellowship, the Anderson Center for Cancer Research fellowship and the *Women & Science* fellowship.

Teresa joined our lab in early 2008 at a time when she was still speaking her charming, but at times challenging, staccato Italian English. She is from Parma and became enormously popular because she would bring us her father's wine and amazingly large chunks of the best Parmesan cheese you can imagine.

Teresa joined the lab because she had a keen interest in cancer research and in fact had already done quite some work in this area with Pier Giuseppe Pelicci in Milan. To explore a cancer-relevant aspect of telomere biology, she focused on the question of how the loss of telomere function contributes to genome instability in cancer. What followed was a breathtaking period in which Teresa ran her own independent research project and demonstrated that shortening of telomeres can drive cells into an aberrant state where they duplicate their whole genome. Because telomeres shorten in the early stage of tumor development, Teresa's observations help explain why so many human cancers have twice the normal number of chromosomes.

Teresa published her findings in *Cell* and *Cancer Cell*, and earlier this year she was awarded the prestigious Weintraub Graduate Student Award for her work. Hal Weintraub was a brilliant scientist and a much-loved mentor. Fred Cross, a member Teresa's thesis committee, had been a postdoc with Hal. He wrote to Teresa when she received the award as follows:

"Re-reading your telomere re-replication paper, I was very struck with the depth and sophistication of the biological analysis — not just 'DNA damage causes over-replication,' but a whole detective story from telomere shortening in hyperplastic cells, to polyploidization and the possibility of aneuploid disasters in cells that survive crisis. Hal definitely would have appreciated the work."

Paul Daniel Dossa

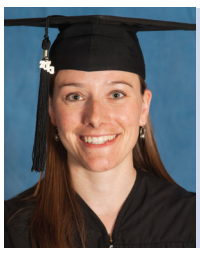
presented by Howard C. Hang

B.S., Harvey Mudd College
Analysis of Small Molecule Inhibitors Aimed at Bacterial Virulence

Humans are constantly exposed to bacteria. The colonization of our tissues with beneficial microbes after birth can help our metabolism and shape our immune system. Unfortunately, we also occasionally encounter harmful bacteria that can cause deadly diseases. As you may know from the World Health Organization and general press, we are running out of ways to treat bacterial infections due to increasing resistance to currently available antibiotics and a limited pipeline of new drugs. My laboratory has therefore been interested in developing molecules that selectively disarm bacterial pathogens without killing the helpful commensal bacteria.

Toward this goal, Paul Dossa was the first graduate in my laboratory to embark on the discovery and characterization of drug-like compounds that can block specific pathways in bacterial pathogens required for infection. During his thesis studies, Paul helped discover and characterize small molecules from medicinal plants that can inhibit infection from bacterial pathogens such as *Salmonella typhimurium*. Paul's thesis work has also helped understand the mechanism of action for other synthetic molecules that can inhibit *Salmonella* infection, which has yielded a new class of drug-like molecules for the development of anti-infectives in the future. His work has paved an important foundation for future studies on anti-infective molecules in my laboratory.

I would like to thank him for his contributions and wish him the best in the future.



Amy Grunbeck

presented by Thomas P. Sakmar

B.S., Dickinson College
Application of Genetically-encoded Photoactivatable Crosslinkers to Map Ligand-binding Sites on G Protein Coupled Receptors

It is a privilege to present to you Amy Grunbeck.

Before coming to New York, Amy received her B.S. degree with honors from Dickinson College in Carlisle, Pennsylvania, where she won the American Institute of Chemists award, which goes to the highest ranked chemistry student each year. Dickinson is a small liberal arts college, but it has a fabulous undergraduate chemistry program. Some of you may not know about Dickinson, but it has a very interesting and relevant history.

Dickinson was founded in 1783 by Benjamin Rush, who was both a physician and a professor of chemistry (not a bad role model), as well as a signer of the Declaration of Independence (even better).

Dr. Rush envisioned a great college at the edge of the frontier (central Pennsylvania was at the edge of the frontier in those days), where both men and women could receive a science-based progressive education. Dickinson remains one of the country's best small colleges.

Well prepared as a chemist at Dickinson, Amy did spectacularly well in her thesis research on a very challenging and important question in pharmacology as it relates to drug discovery. She tried to understand, with chemical precision, how an important class of membrane receptors called heptahelical receptors transmits signals across membranes.

Amy was able to achieve what I feel is a major breakthrough in the field. She applied a new technology called amber codon suppression to introduce a unique type of amino acid that is normally not found in nature into receptors of interest. The amino acids she chose could be coaxed to react with neighboring molecules when exposed to strong ultraviolet light. She used this method to map the interactions between receptors and therapeutic drugs whose sites of binding and modes of action were not previously known.

Amy's method is now widely termed "targeted photo-crosslinking." And it is very cool to chemical biologists.

Amy's work has received significant attention and praise. She has been invited to give platform talks at Banf, Alberta, Canada; San Diego; and at a receptor pharmacology meeting in Brazil. She has also been featured in a "meet the author" interview for a prominent American Chemical Society journal and, in fact, she just shot another video interview two days ago.

Amy's published thesis research forms a substantial coherent body of work that I predict will be taught in chemical biology textbooks in the future.

And on a personal level, Amy has been a pleasure to work with. She has been perhaps the most consistently upbeat and team-oriented member of our group over the past five years — a uniquely talented and likeable person. As she moves to Boston with her husband Carlos, we wish Amy all the best in her future scientific career.

Adam Michael Knepp

presented by Thomas P. Sakmar

B.S., Stanford University
Studies of G Protein Coupled Receptor Stability and Dimerization Using Novel Fluorescence and Crosslinking Approaches

It is a privilege to present to you Adam Knepp.

Adam's thesis research focused on how a particular class of cell surface receptors, called G protein coupled receptors (GPCRs), assemble in the cell membrane with other receptors to form a molecular nanomachine called a "signalosome." He used a combination of computational and experimental approaches to model the disc membrane of the rod cell in the retina at the back of the eye. Adam showed that the light receptor called rhodopsin first forms pairs, or dimers, that then assemble into long rows. The rows then line up side by side forming a type of surface structure that resembles a toy slot car track. The slot between the dimer rows contains lipids from the bilayer.

Transducer proteins inside of the cell can hold on to the track and slide along the slot using their own lipid tails as they carry out a one-dimensional search for a rhodopsin that was activated by light — and only about 1 in 100 rhodopsins are active at any one time even in bright light. Imagine a protein sliding along a molecular slot car track on the membrane surface, and getting knocked off the track once it hits an active receptor — a protein "bump" in the road. Adam's very cool model in part explains the fast physiological response to light in vision.

Adam also developed a very useful enabling technology to measure whether GPCRs are properly folded and how stable they are. Adam's method attracted the attention of biotech and pharmaceutical companies, in part because his relatively low-tech, but clever method needed only about one ten-thousandth of the amount of material that they had been using in their own very expensive biophysical assays to measure basically the same thing.

One company currently using Adam's technology was very surprised when they found out that Adam himself could produce the same amount of data in one week that it took three technicians one month to produce.

Adam's innovative thesis work will continue to pay dividends to future lab members as his methods are more widely applied.

Adam received his B.S. in chemistry from Stanford University. He was a member of the so-called Facebook class. I first came across the term in a *New York Times* article about two years ago. In short, the Facebook class at Stanford was the first class that was given exclusive free access to the Facebook social media application that was being developed just up the road by Mark Zuckerberg after he moved west from Harvard.

When I asked Adam about the Facebook class, he said it was no big deal. Oh … but by the way, he has something like 800 Facebook friends! That is absolutely insane.

Adam is the type of person who never seems to have a bad day. He's an enthusiastic problem solver and always seems to rise to the occasion, for example, as when I asked him to fly to Germany with one day's notice to help with a major presentation at a very contentious meeting.

But Adam is one of the few people I know who has traveled more than I have in the past four years — with carefully planned adventure trips to Kilimanjaro, Machu Picchu and Southeast Asia. He also attended many Stanford Cardinals football games, including key bowl games during the Andrew Luck era.

Adam will start at McKinsey & Company this summer where his enthusiasm and skills will be put to very good use, I'm sure.

Suchit H. Patel *

presented by Sidney Strickland of behalf of A. James Hudspeth

B.S., New York Institute of Technology
Frequency Selectivity of Synaptic Exocytosis in Hair Cells of the Bullfrog's Amphibian Papilla

I will read remarks prepared by Jim Hudspeth who unfortunately couldn't be here today:

One of the most important aspects of our hearing is the ability to recognize the sources of sounds in our environment. In nature, there is an obvious selective advantage in being able to distinguish a prospective meal, perhaps a tasty pig rooting in the bush, from a potential predator such as a lion. With the development of human speech came the necessity to differentiate between speakers, which we can do even in a crowded environment. Still greater refinement underlies our capacity to make aesthetic distinctions between the various instruments in an orchestra. We can distinguish sounds of different origins by their content of particular frequencies or tones. A female voice has a higher range of frequencies than a male voice; a violin is pitched above a viola. And your ability to separate my voice from that of the prior speaker stems from a still finer judgment of the pitches characteristic of individual voices.

These discriminations commence in the cochlea of the inner ear, which functions like an inverse piano to decompose complex sounds into their tonal constituents. Each of the sensory cells in the cochlea is tuned to a specific frequency of stimulation and sends signals about that frequency along nerve fibers into the brain.

Investigating the flow of information from the sensory cells to the nerves, Suchit found for the first time that this interaction is also tuned to specific frequencies. In other words, the chemical synapses at which sensory cells communicate with nerve fibers themselves help us to discriminate sounds. This result, which represents the first demonstration of tuned synapses, will encourage a search for additional examples of the phenomenon in

other parts of the nervous system.

Suchit has long had an interest in clinical medicine as well as research. He earlier worked on several medical problems and encouraged disadvantaged high school students to enter medical careers. He has served as executive director of the Weill Cornell Community Clinic, a voluntary organization that provides medical services to the indigent, and founded the Heart-to-Heart program that offers citywide screening for cardiac problems. As a student in the M.D.-Ph.D. program, he will now complete his clinical coursework. Thereafter, Suchit plans to enter into a clinical career, perhaps in radiology, in which his personal warmth and intellectual acuity will serve him well.

Dennis Justin Spencer *

presented by Vincent A. Fischetti

B.S., Morehouse College
Determining the Phenotypic and Genotypic Response Exhibited by Streptococcus Pyogenes *at the Human Palatine Tonsil*

A child that gets a group A streptococcal infection that is adequately treated will not suffer any major consequences, however a pharyngitis (or strep throat) from the same organism could result in rheumatic fever and rheumatic heart disease. Although intensive research into the cause of rheumatic fever has gone on for decades, a clear picture as to the connection between the throat infection and heart damage is still unclear. One of the research tools used to examine the infection process of streptococci is a collection of human pharyngeal cells in culture, the only cell line available from the human oral cavity. These cultured cells have been used for decades to examine the attachment and invasion of streptococci and the genes responsible for this event. However, streptococci do not infect pharyngeal cells, they specifically target the tonsils causing tonsillitis.

When Dennis Spencer joined my lab he wanted to examine streptococcal interactions with tonsillar cells, to see if they differed from pharyngeal cells. He found that when he used human tonsillar tissues discarded from surgical procedures, the variability in his results were such that clear decisions could not be made. However, like much of science, a bit of luck came his way. In his reading, he discovered a paper in which a surgical group reporting on head and neck cancers identified two cancers in human tonsils. Dennis contacted the authors and received samples of these cells. He then began an extensive characterization and compared them to the pharyngeal cell line. What he discovered was that they were good representatives of tonsillar cells because they had not changed as a result of the cancer. More importantly, the streptococci were able to attach and invade these tonsillar cells 10 times better than the pharyngeal cells. Furthermore, when he examined the streptococcal genes that were turned on during this interaction, he found several candidates that had not been described before.

We believe that this tonsillar cell line will soon replace the pharyngeal cells in further studies of streptococcal infections, and in doing so may point the way to finally understanding the connection between the throat and the heart.

Of all the students and postdocs that I've had over the years, Dennis is by far the best dressed and loves to wear a bow tie on special occasions. On a more serious note, Dennis devotes a lot of his time mentoring students, not only in the lab but also on the national level with his eight-year affiliation with the Student National Medical Association.

Dennis is now very busy doing his clinical studies at Weill Cornell Medical College; in fact they gave him the day off today so he could graduate. I am happy to report that his experience in the lab has turned his attention to ear, nose and throat as his medical specialty.

Chan Lek Tan

presented by Paul Greengard

B.A., Christ's College, University of Cambridge
Tuning of Neuronal Excitation by a Brain Specific MicroRNA miR-128: From Targets to Behavior

Chan Lek Tan is a brave young traveler on a historic path to conquer the Wild West. Born in Malaysia, Chan's first western migration brought him to the United Kingdom, where he graduated with honors from Cambridge University with a bachelor of arts degree in natural sciences. Inspired by his success, he continued his journey toward the west and entered the Ph.D. program at The Rockefeller University. Determined to venture deeper into unknown territories, he joined my laboratory to work with Anne Schaefer on the role of microRNAs in controlling brain function. Chan's research showed that even tiny pieces of RNA can have a huge impact on brain function. In a set of elegant genetic, molecular and behavioral experiments, Chan identified a 25 nucleotide-long microRNA that controls neuronal excitability and functions as a key regulator of motor activity and seizure susceptibility in mice.

Chan's education at Cambridge University gave him not only a sense of irony that he would generously share with his friends and colleagues, but also seeded a deep passion for literature. In order to satisfy Chan's appetite for books without compromising his devotion to his experiments, he became a true devotee of audiobooks. These audiobooks would cause Chan to erupt occasionally with seemingly inexplicable laughter while pipetting at his bench late in the evening. In his free time, Chan likes to travel, enjoys good food and is a great listener.

Chan will now continue his tireless quest westward by pursuing the great unknowns of neuroscience in the distinguished laboratory of Zach Knight at the University of California, San Francisco. As he continues his trip around the world, we wish Chan all the best for his next adventure.

Sarah Van Driesche

presented by Robert B. Darnell on behalf of himself and Jennifer C. Darnell

B.A., Wellesley College
Mechanism of Translational Control by the Fragile X Mental Retardation Protein and Creation of the FMRP cTAG Mouse

Sarah Van Driesche came to The Rockefeller University as an athlete and a scientist, and managed to score an amazing goal during her time in our lab.

Sarah is one of the most ingenuous, careful and committed scientists we have seen in the laboratory. She came here from Wellesley College, with high grades, great GREs, a perfect 900 on her Biology Advanced Subject test and the Fiske Prize in Biology. The latter was for a series of lab projects she did, progressing from interests in anatomy and physiology to more detailed functional analyses at the molecular level. In fact, she herself described her view of the beauty of cellular machinery at the time as "intricate, eloquent, biologically cool as if inspired by Rube Goldberg and Dr. Seuss together." Her mentors described her in terms that were a bit more conventional but no less praiseworthy, for example, as "a gem, with the best hands I have ever seen."

Sarah's work was characterized by extreme focus and attention to detail. This can be seen in perusing back over her original thesis proposal, in which she planned to validate FMRP target transcripts by CLIP, and analyze them in specific cell types. This is exactly what she did, which is essentially unheard of! It may sound sensible, but nearly no student actually makes a plan and sticks to it over the years. In Sarah's case, she did so with a wisdom that produced, with her co-thesis advisor and mentor Jennifer Darnell, what I consider one of the most important discoveries our laboratory has made.

To explain very briefly … the commonest form of inherited intellectual disability, often coupled with autism, is the fragile X syndrome. As opposed to most such difficulties in childhood, the genetic cause of this has been known for over 20 years. A sobering reminder of how hard science is, in all that time no clear understanding of what the fragile X protein did, its relationship to autism or hence a logical window into how to approach these problems clinically had been established. Sarah and Jen worked side by side to execute a breakthrough piece of work. They identified what the protein did for the first time — it bound to specific RNA molecules and regulated their ability to be translated by ribosomes. Sarah deserves the highest of gold stars for sticking with an enormously difficult experimental problem, showing that the fragile X protein blocked translation by forcing the translating ribosomes to stop in their tracks. This work, published in *Cell*, has provided the gold standard for our understanding of how the protein works and offers great insights into possible treatments. Moreover, it led to an exciting and unexpected explanation for the link between the fragile X syndrome and autism and, most recently, is giving insights, amazingly, into schizophrenia. All of these avenues are being pursued by our laboratory and others, and provide a testimony to the extremely special nature of Sarah's thesis work. Both Rube Goldberg and Dr. Seuss would be proud, as I know her whole family is, and most certainly as our whole laboratory is.

Finally, not that this is a prerequisite for graduating from our lab, but Sarah also has produced, in addition to a beautiful thesis during her time here, a beautiful little girl.

Amy Wells Quinkert

presented by Bruce S. McEwen on behalf of Donald W. Pfaff

B.S., Rhodes College
Deep Brain Stimulation to Increase Generalized Arousal in Intact Mice and a Mouse Model of Traumatic Brain Injury

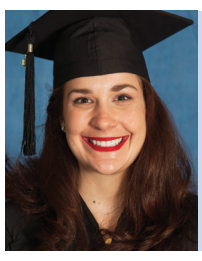
Don Pfaff had an obligation that prevents him from being here. As a member of Amy Wells Quinkert's thesis committee I am delighted to do the honors. Don writes:

The most fundamental and powerful function in the brain is called "generalized central nervous system arousal," essential for consciousness and for the initiation of all human behaviors. Traumatic brain injuries, by car accidents or war injuries, for example, are devastating because they damage generalized arousal pathways in the brain.

Amy Wells Quinkert has addressed these arousal mechanisms during her years at Rockefeller. Just before she began her thesis work, Nicholas Schiff, in the neurology department across the street at Cornell, startled everyone by using deep brain stimulation to provoke the recovery of consciousness of a patient who had been in a vegetative state. Amy, in work that was the first of its kind, demonstrated that the temporal patterning of such deep brain stimulation in laboratory animals could regulate stimulation effectiveness, even when all other physical characteristics of the stimulus pulses were held constant. Her most effective brain sites were in the central thalamus, amongst neurons whose axons project widely to the cerebral cortex. Further, her deep brain stimulation had the effect of changing behavioral patterns from those typical of the animal's sleepy time of day to those typical of the animal's normally active time of day. Thus, Amy could deal with a deep, global brain function in a precise and quantitative manner.

Preparing for Amy's graduation, I was surprised to hear that she has a hobby, knitting. Surprised because, as a typical Rockefeller professor, I thought I had successfully reduced her spare time to zero!

In the race for the Ph.D., Amy has finished ahead of her husband, and when he is ready they'll head for postdoctoral research in Boston.



Laura Winzenread

presented by Leslie B. Vosshall on behalf of Cori Bargmann

B.S., University of Kansas
An Analysis of Synaptotagmins in Caenorhabditis elegans

Cori Bargmann was unable to be here today and I am pleased to present Laura Winzenread on her behalf.

To me, Laura has always embodied the spirit of Dorothy from *The Wizard of Oz*. She hails from Edmond, Oklahoma, and moved to Lawrence, Kansas, to do her undergraduate work at the University of Kansas. There she was a Phi Beta Kappa scholar of genetics, a fly researcher, as well as a proud member of the sorority Kappa Alpha Theta. In 2005, she was magically picked up and deposited at the gates of the Emerald City at 66th Street and York Avenue, an exotic Midwesterner, Jayhawks fan and sorority girl.

In Cori's lab, she carried out a genetic screen to dissect the rules of synaptic organization in the worm. Using a fluorescent marker to tag synapses — the point at which two neurons communicate with each other — Laura screened for worms with aberrant synaptic morphology. This involved many hundreds of hours of looking for tiny faint spots along a worm neuron that changed in a potential mutant. She succeeded in identifying mutations in a gene called *synaptotagmin* as responsible for defects in one of her mutants.

Laura was an enthusiastic supporter of our graduate program, always involved in recruiting students at the spring open house and in one memorable trip back to Kansas, accompanied me to pitch our graduate program to University of Kansas biology majors.

Somehow between her community service at Rockefeller and her intense worm-gazing in Cori's lab, she found the time to appear (and earn $2,300) on a TV game show called "Cash Cab."

This particular Dorothy will not be going back to Kansas but plans to stay in our fair Emerald City to pursue a career in management consulting with the eventual goal of applying her prodigious scientific intellect and magical social skills to equity research in the biotech sector.