7-2010

BenchMarks 2010, July 2

The Rockefeller University

SCIENCE FOR THE BENEFIT OF HUMANITY

BENCHMARKS

THE COMMUNITY NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

FRIDAY, JULY 2, 2010

With the graduation of its 52nd class, the alumni of The Rockefeller University's graduate program now number 1,047. This year's Convocation celebration included a French bistro-themed reception in the President's House, a luncheon, the traditional cap-and-gown procession across campus, a formal ceremony in Caspary Auditorium and a campus-wide celebration in Weiss Café.

The 37 members of the class of 2010 consist of 24 men and 13 women from 18 countries: Argentina, Austria, Canada, China, Fiji, France, Germany, Hong Kong, India, Ireland, Israel, Japan, Korea, Macedonia, Poland, the Russian Federation, Trinidad and Tobago and the United States.

Of the 28 students in the Ph.D. program, 23 will go on to post-docs, one will attend medical school, one will enter an M.B.A. program, one has begun film school and two are considering their options. The nine participants in the Tri-Institutional M.D.-Ph.D. program will return to medical school to finish their M.Ds.

This annual Convocation issue of BenchMarks *salutes the 2010 graduates of the David Rockefeller Graduate Program.*

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

CONVOCATION 2010 FOR CONFERRING DEGREES

Thursday, the tenth of June

PHOTOS: HEATHER LASZLO AND ZACH VEILLEUX

Science, education leaders accept honorary degrees

This year's recipients of honorary doctor of science degrees, Hanna Holborn Gray and Harold E. Varmus, have played major roles in shaping education and science in the United States. Dr. Gray, president emeritus of the University of Chicago, recently retired after 13 years as chairman of the board of the Howard Hughes Medical Institute. Dr. Varmus, a Nobel Prize-winning biologist, is former director of the National Institutes of Health and former president of Memorial Sloan-Kettering Cancer Center. Drs. Gray and Varmus spoke at the June 10 afternoon Convocation ceremony.

A historian with special interests in the history of humanism, political and historical thought, church history and politics in the Renaissance and the Reformation, Dr. Gray was the first woman provost at Yale University. As the first woman president of the University of Chicago, she became the first woman to serve as the chief executive of a major research university.

Dr. Gray received her B.A. from Bryn Mawr College in 1950 and her Ph.D. in history from Harvard University in 1957. She taught at Bryn Mawr and at Harvard before joining the University of Chicago's faculty in 1961. During her career she was dean of the College of Arts and Sciences at Northwestern University, provost of Yale University and acting president of Yale. In 1978, she returned to the University of Chicago and was its president until her retirement in 1993.

PHOTOS: HEATHER LASZLO

Honoris causa. Hanna Holborn Gray, top; Harold E. Varmus, bottom right.

Dr. Gray's acceptance remarks included an overview of the educational legacy of John D. Rockefeller, who founded both the University of Chicago and The Rockefeller University. "We can both be grateful…to have had a founder who recognized the vital importance of institutional independence and of individual competence and freedom in the development and strength of great centers of learning and discovery," she said.

Dr. Varmus majored in English literature at Amherst College and earned a master's degree in English at Harvard University. He graduated from Columbia University's College of Physicians and Surgeons, worked as a medical student in a hospital in India, and served on the medical house staff at Columbia-Presbyterian Medical Center. His scientific training occurred first as a Public Health Service officer at the NIH and then as a postdoc at the University of California, San Francisco.

Much of Dr. Varmus' scientific work was conducted during 23 years as a faculty member at UCSF Medical School, where he and his colleagues demonstrated the cellular origins of the oncogene of a chicken retrovirus. Dr. Varmus is also widely recognized for his studies of the replication cycles of retroviruses and hepatitis B viruses, the functions of genes implicated in cancer and the development of mouse models of human cancer.

Dr. Varmus's remarks explored the tension that is inherent in scientific research: the competing goals of trying to make one's mark as a scientist while the scientific community as a whole validates a discovery through consensus. "Ultimately, the goal is to help shape the way the community thinks, our current views of nature, and to establish values in science we as a community can espouse," Dr. Varmus advised.

BENCHMARKS

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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 percent postconsumer waste.

Teresa Davoli awarded David Rockefeller Fellowship

Teresa Davoli has had a powerful interest in cancer biology since high school, when she started scouring books on the subject. She's inspired by efforts to find treatments for the deadly diseases that target specific molecular interactions, as opposed to the relatively blunt carpet bombing of chemotherapy. Ms. Davoli is pursuing that aim as a member of Titia de Lange's Laboratory of Cell Biology and Genetics. For her research accomplishments and contributions off campus as well, she was awarded this year's David Rockefeller Fellowship.

A native of Parma, Italy, Ms. Davoli earned her bachelor's degree in molecular biology from the University of Pisa and a master's in medical biotechnology from the FIRC Institute of Molecular Oncology at San Raffaele University in Milan. On the advice of her mentor Pier Giuseppe Pelicci in Milan, and after an encouraging visit with Rockefeller's Elaine Fuchs, Ms. Davoli joined Rockefeller in 2006. Following a rotation in Dr. Fuchs's Laboratory of Mammalian Cell Biology and Development, Ms. Davoli took a turn in Dr. de Lange's lab, where she "got lucky" with the results of her initial work, on the molecular basis of genomic instability. She decided she wanted to see the project through.

PHOTO: HEATHER LASZLO

Fellowship festivities. David Rockefeller congratulates fellowship recipient Teresa Davoli at the Convocation luncheon.

Ms. Davoli is studying telomeres, the structures that cap and protect the ends of chromosomes. In what Dr. de Lange describes as "a breathtaking period of two years," Ms. Davoli worked out how telomere dysfunction leads to chromosomal aberrations that can cause cancer. The experiments were published by *Cell* in April. Now she wants to find out whether her discoveries about telomere dysfunction in various model systems apply in people as well, and she's collaborating with a pathologist at Memorial Sloan-Kettering Cancer Center to that end. "I'm really interested to see whether this has implications for human tumors," she says. "That's the challenge now."

The laboratory doesn't consume all of her energy, however. Since her college days, Ms. Davoli has volunteered with the Community of Sant'Egidio, an international organization that reaches out to disadvantaged or underserved communities. In Italy, she taught biology to young students. Now, in New York, she makes weekly visits to nursing home patients and advocates for them with social service providers. She has been a *Women & Science* Fellow. And as an Anderson Cancer Center Graduate Fellow, she helps organize the annual Anderson Cancer Symposium at Rockefeller. She is also a regular participant in Genome Integrity meetings at the New York Academy of Sciences.

Ms. Davoli did not think much of it this spring when Dr. de Lange asked for a copy of her curriculum vitae. When Sidney Strickland, dean of graduate and postgraduate studies, called her in the lab about two weeks later and asked if she could come to his office — right then — she worried. "He said it was nothing bad, but still, it was a little scary." The news that she had won the fellowship was a welcome surprise.

"Teresa is an extremely gifted scientist who is active outside of the laboratory," says Dr. Strickland. "Her devotion to her research and also community service is very much in keeping with the ideals of the David Rockefeller Fellowship."

Teaching awards honor Gilbert and Rice

Charles D. Gilbert, head of the Laboratory of Neurobiology, and Charles M. Rice, head of the Laboratory of Virology and Infectious Disease, were the recipients of this year's Rockefeller University Distinguished Teaching Awards. Established in 2005 to recognize outstanding individual contributions to the university's educational environment, the teaching awards are presented each year to one or two faculty members. Chosen by a committee that includes the university's scientific executive officers, awardees receive a plaque and a monetary gift. Dr. Gilbert (below) teaches a course on neural systems that covers mechanisms of information processing in the adult nervous system at the level of neuronal ensembles and interactions. Dr. Rice is the primary organizer of a virology course that covers virus structure, replication, molecular genetics and gene expression, interactions with host cells, immunology, pathogenesis, viral vaccines, antiviral therapy and resistance and viral vectors. The awards are presented by the president each year during the Convocation luncheon. (Dr. Rice was traveling and was not available to receive the award in person.)

PHOTO: HEATHER LASZLO

Following tradition, faculty mentors gave congratulatory tributes to this year's graduates. Following are the transcripts of those speeches, as they were read on June 10. Two members of the class of 2010 — Evan Feinberg and Eileen Woo — were unable to attend the festivities. Students in the Tri-Institutional M.D.-Ph.D. Program are marked with an asterisk.

Maya Bader

presented by Hermann Steller

B.Sc., Tel Aviv University

Mechanisms of Controlled Proteolysis during Drosophila *Spermatogenesis: Coordinate Action of Apoptotic Caspases and the Ubiquitin-Proteasome System*

It is with great pleasure, but also with some sadness due to her upcoming departure, that I present Maya Bader. Maya has been a spectacular student who will leave a big, empty hole behind here.

Maya received her B.S. in biology and biotechnology from Tel Aviv University in Israel in 2004 and joined Rockefeller in the fall of that year. For her thesis research, Maya investigated how the machinery that is normally used for programmed cell death can be employed to drastically alter the shape and size of cells. All our cells have the ability to self-destruct by activating an intrinsic cell suicide program, which is important to remove any unwanted and potentially dangerous cells, such as cancer cells. However, this cell death program can also be used for non-lethal purposes, such as cellular remodeling.

The particular model that Maya studied is sperm differentiation in *Drosophila*. Sperm cells are unusual in many ways: they are long, thin and very light "minimalistic" cells designed to efficiently deliver their genetic material to the egg during fertilization. But sperm are derived from big, round precursor cells. So for sperm to become lean, efficient swimmers, they have to "slim down" and loose the vast majority of their cytoplasm and organelles, and this is achieved, at least in part, by using the cell death machinery.

In her research, Maya discovered a novel connection between the cell death program and the machinery devoted to the degradation of cellular proteins, a nano-machine termed the proteasome. The conventional view has been that proteasomes are like shredders that are always running, and that proteins get fed into these shredders after they have been tagged with a small protein called ubiquitin. Maya discovered a completely new mode of proteasome regulation that reveals that the activity of proteasomes can actually be modulated. All the components and interactions that Maya has studied are conserved between flies and humans, indicating that her results will have broad, general significance. Her results are not only relevant for sperm development, but also guide our views on remodeling of other cell types, such as nerve cells, which can also undergo major structural changes.

Maya's discoveries are exciting because they reveal a fundamental new regulatory principle, but they also have important medical implications. The proper turnover of both proteins and cells is critical for our well-being, and many human diseases are associated with defects in these major degradation systems, including cancer, neurodegenerative diseases, muscle wasting and many more. Therefore, Maya's results may ultimately enable us to develop new therapies to treat these diseases. Maya has already published several important papers, and she is now working on the final revisions of another high-profile article.

In sum, Maya made invaluable contributions, both through her discoveries which led to an entire new line of research in my laboratory, but also through her wonderful positive and fearless approach to science. She has been a model and inspiration to others in the lab, and a highly valued colleague to me. We will miss her very much. But Maya is off to a very bright future and will soon move to Los Angeles to start postdoctoral research in Larry Zipursky's lab at UCLA in California. There she will study other types of long cells, nerve cells, and apply her knowledge and skills to important questions in developmental neurobiology. I predict that Maya will continue to excel and that she will become one of the leaders in biomedical research. So it is both with great pleasure, but also with considerable sadness thinking of her upcoming departure, that I present Maya Bader.

Amrita Basu

presented by C. David Allis

B.S., Cornell University

Computational, Biochemical and Genetic Studies Aimed at Predicting the Acetylome

When I first was introduced to Amrita Basu by Eran Segal, who co-mentored Amrita's doctoral research in the Tri-Institutional Computational Biology Program, I wasn't sure where I fit into the picture. In short, it *didn't compute*. Fortunately for me, it *did compute* for Amrita, and with more conversations, the decision was made to explore whether computational methods could be used to better define and to predict the protein acetylome in yeast and humans. Drawing upon her strong background as an electrical engineer, Amrita developed a "PredMod" program that computationally predicts post-translational modifications, not only in histone proteins, but also in non-histone proteins. Protein acetylation, the primary focus of Amrita's research, has recently been reported to be as widespread in biology as protein phosphorylation. In response to Amrita's published studies, Jerry Workman and colleagues wrote in *Nature Biotechnology*, "The true size and complexity of the acetylome is being revealed, contributing to the identification of new targets for therapeutic intervention."

Taking a yeast genetics course at Cold Spring Harbor, Amrita turned herself into a wet-lab molecular geneticist, attempting to better define the "rules" of protein acetylation, through the targeted mutagenesis of residues flanking the acetyl-lysines predicted by her computational work. We look forward to learning how Amrita will combine computational and molecular biological approaches in her future postdoctoral studies at Novartis (and her pending marriage!). Whatever she does, inside or outside of science, it will be done with a wonderful smile and positive attitude. For now, "so long, farewell," Amrita, but always stay in touch.

Jacob T. Bendor

presented by Sidney Strickland on behalf of Paul Greengard

B.S., Tufts University

A Molecular Mechanism for Endocytic Recycling of the M5 Muscarinic Acetylcholine Receptor

Jacob Bendor could have chosen to pursue a career as a professional musician during his early years in Boston playing saxophone, flute and guitar with a dash of piano. He could have been a great chef mixing flavors and spices, as he loves picking the best produce to create elaborate, sophisticated dishes. Instead, even though he kept mushrooms as his inspiration, he chose the laboratory bench over the kitchen counter, pipets and pipetmen instead of whisks and wooden spoons, mixing agonists and antagonists.

When Jacob joined our laboratory, we were about to initiate a new program on the muscarinic acetylcholine receptor, an important class of receptor activated by muscarine, a natural molecule found in various mushrooms. The goal of Jacob's project was to study how muscarinic acetylcholine receptors modulate dopamine signaling in the brain. Jacob set out on a very challenging and ambitious project. He took it on without hesitation and initiated the project from scratch, not choosing one receptor but instead choosing the entire family. After meticulously developing a powerful series of tools and reagents necessary

for these studies, he remarkably succeeded in showing not only how muscarinic acetycholine receptors regulate dopamine in vivo but also how they work mechanistically at the molecular level. Jacob, with a perfect balance between persistence and determination, not only studied the receptors themselves but he also developed new protocols, especially one bringing transfection efficiency of primary neuronal cultures to a new level.

Besides all these qualities that are essential for a scientific career, Jacob has an extremely kind and generous personality (which we already miss), an encyclopedic knowledge and a great sense of humor.

Jacob will be moving to the West Coast where he will investigate the normal functions of the Parkinson's disease-related protein alpha-synuclein with regard to neurotransmitter release and synaptic vesicle biology.

In closing, as you have no doubt realized by now, I am sure that Jacob has learned a great deal during his time at Rockefeller, but there is one thing that we were not successful in teaching Jacob — and that was to forget about the Red Sox and become a Yankees fan.

Shyam Bhaskaran

presented by C. Erec Stebbins

B.Sc., The University of Sydney
M.S., San Francisco State University
Structural and Functional Characterization of Bacillus anthracis *UDP-G1cNAc 2-Epimerase and Salmonella Secreted Effector I*

It is my great pleasure to present to you today Shyam Bhaskaran. Shyam came to my lab with a reputation from other faculty as one of the brightest students in his class. He also came with a background of three years in industry, making him unusually experienced at the bench for a student.

Shyam focused on two projects during his thesis work. The first was related to his interest in drug development, and he worked initially with a departing postdoc on an enzyme from gram-positive bacteria critical to synthesizing the cell wall of several human pathogens. He quickly identified critical flaws in an assay we had been using to characterize this enzyme, and which we were close to trying to publish. This detective work relied on both his innate intelligence and his experience in enzymatics.

Shyam went on in a collaboration with the Fischetti lab here at Rockefeller to use the new assays he developed to screen potential drug compounds and help in the discovery of a novel class of small molecules that stop the growth of numerous bacterial pathogens, including drug-resistant staph, strep and anthrax. Several of these molecules are now in animal trials, and showing great promise.

The second component of his thesis involved understanding a factor from *Salmonella* that promotes its systemic spread throughout the body. *Salmonella* can infect macrophages, immune cells of the body that are mobile to hunt down invading organisms. The protein Shyam studied was known to reprogram macrophages containing *Salmonella* to disperse themselves rapidly throughout the body, and not stay at the site of infection. The bacteria hitch a ride on these immune cells and thereby can invade many tissues.

Shyam used a technique called X-ray crystallography to develop images of this protein in which every atom in this molecular machine can be precisely placed. This blueprint of the virulence protein allowed him to determine that it had a very specific chemistry, suggesting modifications of signaling molecules regulating cell structure. For the first time, the powerful activity of this protein could be understood from the ground up, connecting the induced macrophage dispersal to the regulation of biochemical pathways in the cell.

If there were more time, I could also tell you many interesting things about Shyam outside of his scientific work, such as his vampiric sleep/wake cycle, his passionate pursuit of martial arts, and his great stories of overcoming bullies that would impress even Bruce Lee.

Shyam's continuing interest in the concrete application of science to medicine has now led him to an accelerated M.B.A. program at Cornell University. He plans to combine his knowledge of science, his experience in industry, and his soon to be honed business skills to biotechnology.

We wish him all the best in this next stage of his career.

Patrick Bhola

presented by Sanford M. Simon

B.A.Sc., University of Toronto
Variability and Dynamics of Apoptotic Events in Single Cells

Patrick Bhola joined my lab less than five years ago
After living his whole life up in Toronto
He was quick at the bench, he rarely said no
With his smarts and his drive he was clearly a pro

We knew that his interests were wide, with great breadth
But was it all triggered from reading Macbeth?
That led him to spend his time studying death
Following cells as they took their last breath?

There are many reasons for why cells must die,
It hits normal cells in the blink of an eye
Cells transformed, infected or just gone awry
All this Patrick would probe with a fluorescent dye

In school he was trained as a crack engineer
So he brought that old mindset to his new career
He designed two new probes in his very first year
With signal-to-noise, Roger Tsien would revere

To understand death was his cause to embrace
His experiments quickly filled up our disk space
He moved into the lab determined to chase
The mysterious behavior of the enzyme caspase.

So after many years work, what's the fruit of his labor?
When one cell died, so did its neighbor!
What was delivering this deadly saber?
This was the task that he did belabor

We thought something secreted would be the linchpin
That thought was wrong, much to our chagrin
It was not just proximity, it must be its kin,
When one cell died, so did its twin.
As Patrick soon found, he'll tell you with a grin
The secret to life and to death lies within.

So now Patrick it's time for us to say goodbye
I am sure that you always will reach for the sky
Just remember when you see things with your mind's eye
Even that can be done with a fluorescent dye.

Postscript: Patrick Bhola has started postdoctoral work at Dana Farber in Boston.

Matthew J. Bick

presented by Seth A. Darst

B.S., University of Rochester
Structural Studies on the Regulation of Sporulation in Bacillus

I have the pleasure of introducing Matt Bick. Matt has an unusual background, even for a Rockefeller graduate student. He started his undergraduate career as a music major at the Eastman School in Rochester, one of the top music schools in the country. He graduated from Rochester, but with a degree in microbiology. From there he worked as a technician in the Rice lab here at Rockefeller. He joined the graduate program in 2003 and my lab soon after.

Matt also had one of the most unusual lifestyles for a graduate student. For most of his existence here, he ate like his other budget-minded student colleagues and friends, even stooping so low as to eat sandwiches from the A-level vending machine. Every once in a while, though, Matt's father would visit for a few days at a time, and Matt would eat several meals a day at the top New York restaurants. Fortunately, these binges would be infrequent enough to allow Matt's cholesterol count to come back down to normal.

In fact, when you get to know Matt, you learn he is a man of extremes. He doesn't really consider something a real rock concert unless it involves fake blood on the stage. He doesn't really consider a Bach fugue worthy unless it has at least six voices. You get the idea.

Matt's approach to science is similar — Matt's always striving to do the best, and it's been a real pleasure having him as a colleague.

Sung Wook Chi

presented by Hermann Steller on behalf of Robert B. Darnell

B.S., M.S., Korea University
Genome-wide Decoding of mRNP and miRNA Maps

It is my pleasure to put down these words of testimony to a fantastic scientist and colleague, Sung Wook Chi. I am of course sorry that I cannot be present in person for Chi's graduation, but am in the happy and somewhat ironic position of currently being in Seoul, Korea, singing his praises in a series of lectures on his home turf.

Chi came to The Rockefeller University very accomplished, with a master's degree and publications in such varied journals as *Machine Learning*, *Genomics & Informatics* and *The Journal of Cell Biology*. This immediately tells of his unusual nature, a blend of biology and bioinformatics, one that he carried right through during his Ph.D. work.

The Nobel Prize was given in 2006 for the discovery of small RNAs, which are a clear exception to the maxim that size matters. Despite their little size, these RNAs play a big role in regulating gene expression and hence cellular function. Yet despite their certain importance, a clear understanding of their biology has remained elusive. Trying to understand where the little devils bind is difficult, as they are not only short to begin with, but to work they need to bind only very little stretches of their sequence to cellular mRNAs — meaning that they can potentially bind all over the cell's transcripts. Bioinformatics alone has failed to adequately predict where they bind to mRNA, and figuring out this key to the function of small RNAs was the task Chi undertook for his Ph.D.

Chi's approach harked back to his root interests, blending bioinformatics with rigorous biochemistry. He applied a new method our group has worked out, termed HITS-CLIP, covalently crosslinking all of the little RNAs present in the mouse brain to their protein regulators. With these links in hand, he made a remarkable and unexpected breakthrough, finding that a three-way link could be made — between the little RNAs, their protein regulators and the surrounding mRNA sequences which they were regulating. These experiments, yielding literally many millions of small sequences, required some serious computational work to decipher. But in the end, that is exactly what Chi was able to do — decode the precise position at which small RNAs — essentially all of the brain's microRNAs — bind to the brain's many individual mRNAs. This absolutely beautiful work was published as a full article in *Nature*, and as with all such breakthroughs, revealed not only the hoped for — rigorous maps of small RNA binding sites — but a plethora of new and unexpected findings about the little devils. This is work he has followed up in a second complex paper describing brand new rules of small RNA biology, work that is currently being submitted as another major publication, as well as in new studies he is pursing as a postdoctoral fellow in Greg Hannon's laboratory. We know that Chi will continue to shine in his new lab, and we wish him the greatest continued success in the rising star of his career going forward.

Chad Euler

presented by Vincent A. Fischetti

B.S., The University of Vermont
The Role of Lysogenic Bacteriophage in Virulence and Survival of Streptococcus pyogenes

Bacteriophage, or phage for short, are viruses that infect bacteria. Two facts about phage: (1) there are ten times more phage than bacteria on Earth; and (2) the toxins responsible for diseases like scarlet fever, whooping cough, food poisoning, etc. are caused by bacteria that carry toxin-producing bacteriophage.

When you look into the genome of most bacteria, particularly disease bacteria, you find the genome of phage. In *streptococci* that cause human disease you could find from three to eight different phages sitting in their genomes. Chad Euler wanted to know what role these phages play in the disease capability of group A strep, the organism responsible for strep throat, rheumatic fever and flesh-eating disease, among others.

In order to answer this question he needed to excise the phage genome precisely, such that he restored the strep genome back to its pre-phage state. It's not an easy task and has never before been accomplished.

Chad devised a strategy and set out to systematically remove all four phage from a group A strep strain, which took many months of hard work. In the end he had a *streptococcus* that was completely devoid of bacteriophage, an organism that does not now exist in nature, but perhaps did millions of years ago.

When he compared the characteristics of the phage-containing strain with the minus strain he found some exciting differences that are and will be important in our understanding the disease capability of *streptococci*. However, I do not have time to go into it in detail.

Chad is also creative in his non-scientific life. He and his then-girlfriend Tara were on

"Live with Regis and Kelly" and took first prize for the most creative Halloween costume — Chad was a fisherman and Tara a mermaid — but how it was done defies description. Just picture a Gorton fisherman holding a mermaid, her tail in his hands but her feet in his pants.

He soon proposed to Tara and they married thereafter and just recently they had a beautiful daughter Avery, who was an integral part of his last Halloween costume.

Chad will stay on in the lab to continue some very promising experiments. Spores are the dormant state of many bacteria such as *Bacillus anthracis*, the organism that causes anthrax. This bacterial form is highly resistant to harsh environments and can survive for decades in this dormant state. When a suitable environment is encountered the spore germinates to the living bacterium. The spore has multiple layers to allow it to survive in different environments, the outermost layer, the exosporium, being the one responsible for direct interaction with specific surfaces. Some spores have appendages for other types of interactions.

Monica Fazzini

presented by Vincent A. Fischetti

B.S., University of Buenos Aires
Exosporium Morphogenesis in Bacillus cereus *and* Bacillus anthracis

Monica Fazzini came from Argentina and was interested in the outermost layers of the spore, since understanding them better will allow us to control spores and perhaps prevent disease. One of the more interesting things that she found was that the appendages were composed of a protein that is resistant to the harshest chemical treatments, making it impossible to break down to its basic units, thus making it one of the most resilient proteins ever described. In her studies, she also identified a new gene that was responsible for controlling the synthesis of the exosporium. Her experiments clearly showed that the exosporium is important not only in protecting the spore from environmental insults such as enzymes but is responsible for the proper production of the spore and the timing responsible for germination to the bacillus form, all of which would be important for spore survival and, as such, targets for intervention.

Monica did not work all the time; she did find time to meet Peter, who she married just a year ago. Now we noticed that she smiles a lot.

Monica and Peter will move to Washington, DC, in the fall to continue each of their careers. We will miss her bubbly personality, particularly during lab parties.

Alexis Robert Gambis

presented by Hermann Steller

B.A., Bard College
M.S., University of Marne-La Vallée
Cell Death in Drosophila *Photoreceptor Neurons*

Alexis Gambis was born in Paris and moved to New York in his late teens, where he became fascinated by how science and technology intersect with life and people. He received his B.A. from Bard College in upstate New York in 2003, followed by a master's in bioinformatics from the University of Marne-La Vallée in Paris, France, in 2004, and came to The Rockefeller University that year.

It seems Alexis' life revolves around vision, in both science and the arts. His parents are distinguished artists, a painter and filmmaker, respectively, and he himself combines unusual talents as an artist and a scientist. Actually, many of you may have first gotten to know Alexis from his various activities in making and promoting films here in the Rockefeller community. But on the days and nights when Alexis was not making a film, he studied the mechanism by which differentiated photoreceptor neurons in *Drosophila*, the cells that receive light and mediate vision, undergo cell death. These nerve cells, like virtually all cells of higher animal, can activate a cell-suicide program to self-destruct. Having such a program is very important since it serves, amongst other things, to remove damaged and potentially dangerous cells, including cancer cells. Better dead than wrong: from an organism's perspective, it is better a cell dies than takes a chance that it becomes a troublemaker. But this cell-suicide program can become a liability and contribute to the loss of cells that we would like to keep, which is particularly problematic in the nervous system. Using the fly visual system as a model, Alexis investigated how nerve cells deal with oxidative stress, which is a known mediator of neuronal cell death. In particular, Alexis showed the critical importance of antioxidant defense systems, specifically ferritins, which are proteins that bind iron and keep it in a less reactive state, for protecting against cell death. So this may serve as a warning to be careful with these iron supplements! His work involved making reporters for live imaging of these stresses in living cells, and he initiated a genetic screen that has led to the identification of several new players and components in the pathways leading to neuronal death. The detailed analysis of this material will keep another generation of students and postdocs busy, and is very likely to significantly advance our understanding of cell death pathways, which ultimately may lead to better prevention and cures for these devastating diseases.

Since completing his research last year, Alexis has moved on to a new career, in filmmaking. He joined the highly prestigious graduate program at the NYU film school (their acceptance rate is less than three percent). Alexis is also the artistic director of the Imagine Science Film Festival, the first science film festival on the East Coast. Alexis' goal is to enhance public understanding of science and technology, and he also tries to make us scientists look a little more human through visual storytelling. I think we all have a lot to gain by his efforts, and I personally wish him well and continued success in his career.

Aaron David Goldberg*

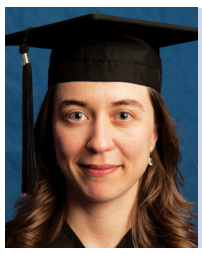
presented by C. David Allis

A.B., Harvard College
Genome-wide Localization and Novel Deposition Pathways of Histone Variant H3.3 in Embryonic Stem and Neuronal Precursor Cells

Every student should have a scientific dream early in their graduate career. Big ones are good, and arguably, bigger ones are better. Aaron Goldberg is a big dreamer, but to his credit, he has realized his scientific dreams. Histone genetics can't be done in mammalian cells because there are too many gene copies, but that didn't stop Aaron from thinking of clever ways to get around that problem. Genome-wide studies were not routine for the Allis lab, leading Aaron to say, "So what, I can do this." Does Aaron have a secret weapon that helps to shape his many successes in the lab? Absolutely. Aaron has an unbridled enthusiasm for everything he does, an enthusiasm that rivals my own (now that's a scary mix).

How many students can claim that they know almost everyone at Rockefeller or in the Tri-Institutional neighborhood? Many perhaps. But how many students have been so enthusiastic they have gotten most of them to work for them in pursuing a remarkably ambitious set of thesis goals? Few, would be my guess. Armed with his infectious enthusiasm, Aaron has left a long-lasting imprint on many of us. As a tribute to Aaron and his work, at least five current members of my lab are following up on various aspects of Aaron's thesis work — not too shabby.

In closing, Aaron has been an exceptional student, leading me to conclude that he will go on to do many more exceptional things, not only in his own lab someday, but with his patients. If I was choosing a "real doctor" to take care of me, Aaron would be high on my list. If I was choosing a lab to do a sabbatical someday, it might be Aaron's, if he has room. Good show, Aaron! What a fun ride it has been with you.



Elizabeth Goneska

presented by C. David Allis

A.B., Mount Holyoke College
Characterization of Histone H2A Functional Domains Important for Regulation of the DNA Damage Response

Elizabeth Goneska began her doctoral studies studying DNA damage in the ciliated protozoan *Tetrahymena*, investigating whether an "epigenetic signature" could be better defined for broken DNA. Elizabeth soon recognized that budding yeast provided her with an easier route to look for mutations in histone genes that might give rise to DNA damage phenotypes. Elizabeth's mutagenesis work was framed by the fact that a single point mutation in a well-known phosphorylation site in the DNA damage "sensor" H2A.X fails to give a strong DNA damage phenotype, suggesting functional redundancy of other, yet unknown damage-related marks. Teaching herself yeast histone genetics, Elizabeth then moved through both the amino- and carboxy-terminus of yeast H2A, mutating essentially every possible post-translational modification site.

While most graduate students buckle down during their doctoral studies, Elizabeth's research quickly taught her that she needed to "knuckle down." Her in-depth mutational analyses in the histone H2A gene led her to a short stretch at the base of the H2A N-tail, known as its "knuckle region." In pursuing H2A's knuckle region, Elizabeth turned to many of the major assays used to evaluate DNA damage phenotypes. The generally stubborn nature of this histone to reveal all of its secrets proved to be a challenging experience for Elizabeth, but no one can argue that she hasn't given histone H2A a good run for its money. She now hopes to look for epigenetic signatures that dictate function in the mammalian brain. This doesn't sound easy either, but she is a determined individual. We wish her well in all that lies ahead.

Neeraj Kapoor

presented by Thomas P. Sakmar

M.Sc., Indian Institute of Technology, Kanpur
Unzipping Amyloid Fibrils: How a Novel Calcium-binding Protein, NUCB1, Prevents Formation of Amyloid Fibrils

A native of New Delhi, India, Neeraj Kapoor received his earlier training at the Indian Institute of Technology and the National University of Singapore. Neeraj initially went to work trying to understand, with chemical precision, the inner workings of G proteins — proteins that couple to serpentine cell surface receptors and transmit signals. He solved crystal structures of a series of G proteins that he engineered to activate even in the absence of receptors. Neeraj then identified a calcium-binding protein that might regulate G protein signaling pathways. But the real impact of Neeraj's thesis work stemmed from a serendipitous discovery — the type of unexpected discovery that might happen once in a career, if at all.

He noticed an obscure paper in the scientific literature suggesting that his protein might affect the expression level of another protein called amyloid precursor protein, or APP. Neeraj knew that APP was a normal cellular protein that sometimes gets degraded abnormally. He also knew that a particular degradation product of APP, a peptide called Aβ42, was associated in some way with the pathology of Alzheimer's disease.

In fact, one hypothesis is that Alzheimer's disease is caused by an accumulation of Aβ42 that goes on to form what are called Alzheimer's plaques. Plaques are the visible manifestation of a chemical process called amyloid fibril formation. Whereas the individual Aβ42 peptides are minute and invisible, even to high-powered electron microscopes, the Aβ42 fibrils are large enough to see easily. The fibrils assemble progressively over time and once formed, they persist. Some scientists think that the Aβ42 fibrils cause Alzheimer's disease directly — others think that the fibrils are secondary to some underlying disease process. But what is clear is that the fibrils themselves, and even smaller units of assembled Aβ42 peptides called proto-fibrils, are highly toxic to cells. The fibrils can kill neurons.

Dr. Kapoor set about planning experiments to test his hypothesis that his protein could bind to Aβ42. Working primarily with a postdoctoral fellow, Ruchi Gupta, Neeraj made an engineered form of the protein that could stop the aggregation of Aβ42 and decreases its neurotoxicity. Simply put, add Neeraj's protein, and Aβ42 never forms fibrils. Even more remarkable was the discovery that it can actually cause preexisting fibrils to disappear.

Neeraj's finding was unexpected and highly significant and changed the course of work in my laboratory. In the two years or so since their initial observations, Neeraj and Ruchi have tried to understand how the process works. They have also laid the groundwork for developing their discovery as a potential therapeutic agent.

On a personal note, Neeraj is one of the most doggedly persistent, patient and unflappable people I know. He has a temperament well suited to the world's second most popular sport. No, not baseball. Cricket.

Since 2007, Neeraj has played 31 games for the Mad Dogs, a Greenwich-based traveling team that attracts players from all over the Tri-State area. He's known as an "all rounder." He's a very aggressive batsman who doesn't worry too much about fine technique. He scores his runs quickly, and lives dangerously. In total, he's scored 446 runs for the Mad Dogs club with an impressive strike rate of 81 runs per 100 balls faced, and a high score of 47, achieved last year. As a bowler, Neeraj used to run in hard and deliver the ball as quickly as possible, but often with his targeting radar a bit off. Last year, roughly coinciding with his scientific discovery, he calmed down a bit on the pitch and bowled with greater control and a considerable increase in his effectiveness.

When I asked for an assessment from an avid British cricketer, who has seen Neeraj play, he described Neeraj as "adequate," which in this case really means he's fabulous.

Fabulous cricketer. And a fantastic scientist.

Eimear Kenny

presented by Jan L. Breslow

B.A., Trinity College, University of Dublin
M. Res., University of Leeds
Genome-scale Genetics: Lessons from Founder Populations

It is my pleasure to introduce Eimear Kenny upon the occasion of her graduation. Eimear is originally from Ireland and received her undergraduate degree from the University of Leeds in England. After graduation she went to Cal Tech where she worked in bioinformatics as a programmer for the *C. Elegans* Model Organism Database, and did a Master's thesis in ontology development and information retrieval.

In the fall of 2005 Eimear entered the Cornell-Rockefeller Computational Biology Ph.D. program. After spending a year doing coursework at the Cornell campus in Ithaca, she came to NYC to do her thesis work. At the time, Jeff Friedman, Markus Stoffel and I had been involved with the Kosrae study for about 10 years. We had been using linkage analysis to find genes contributing to lipid abnormalities, hypertension, obesity and diabetes, but to that point had experienced limited success. However, we were excited by the prospect of applying a new technology, just then on the horizon, involving high-density SNP chips, to the Kosrae study. This technology would allow the use of genome-wide association, a much more powerful technique for finding genes in populations. Eimear came to see me because of her interest in the genetics of lipids, and became interested in applying this new approach to the Kosrae study as her thesis project. She was involved from the beginning in using the chips to glean the SNP data, and then in the development of new analytical tools in statistical genetics to make use of this information. For the latter, Eimear was guided by Itsik Pe'er, an expert in statistical genetics who is a faculty member in the computer science department at Columbia. With Itsik as her thesis co-advisor, Eimear has been able to develop and apply new methodologies for family based GWA analysis to the Kosrae dataset, and has discovered novel genes regulating risk factors for coronary heart disease.

Eimear is a very likeable, straightforward person, who works hard and is especially adept at multitasking. The latter trait has been of great benefit, since in addition to her own scientific work, Eimear has played a central role in improving and maintaining the Kosrae data base and facilitating its analysis by many other investigators. Without Eimear the Kosrae project would not have moved ahead as it has, and it is hard to imagine going forward without her. Nevertheless, Eimear begins a postdoctoral fellowship at Stanford in the laboratory of Carlos Bustamante, where she will continue her work in figuring out the genetic basis of complex traits in humans. We are sure she will be successful and wish her the very best.

Lee Maxine Kiang*

presented by Paul Nurse

B.A., Yale University
Controls over S-phase and over Nuclear Synchrony

As soon as I met Lee I could tell she was a New Yorker. Something to do with her black pointy-toed shoes and her Zagatpaedic knowledge of New York restaurants. Brought up on the Upper West Side and schooled at Stuyvesant High School, she escaped briefly to Yale before scampering back to Weill-Cornell and Rockefeller for her M.D.-Ph.D.

Bravely she chose to work on yeast. As an M.D., I think she thought yeast was simple enough to be cured of all its diseases. She became interested in how the DNA becomes precisely copied every time a yeast cell divides thus ensuring that every cell receives a full set of genes. To investigate this she studied mutant cells which make too much DNA and unequally copy their genes.

And she made an important discovery. She found that certain regions of the DNA where the copying starts, we call them origins, have a tendency to start making DNA copies more often than they should. When this happens the genes around those particular origins become amplified. It's awkward for yeast but potentially catastrophic for us, because gene amplification can cause cancer.

Lee's experiments often required long time courses. You always knew this was happening because she would arrive early in the morning dressed down for the task, with a mountain of food, particularly very large salads always with arugula and never iceberg.

She also became our very own laboratory doctor. All of us would consult Dr. Lee about our minor scratches, our backaches, our runny noses. All of us would feel much better when she told us not to worry, you will feel better tomorrow. Lee still visits us, now wearing green pyjamas, I think they are called scrubs. But we miss her — we miss her bubbly enthusiasm, her restaurant summaries, her long time courses, our medical consultations, and of course her pineapple and yogurt and her sundried tomatoes.

Thank you Lee for being such fun and all the best in your career as a doctor.

Łukasz Kowalik

presented by A. James Hudspeth

B.A., M.Sc., Trinity College, Cambridge University
Cellular Signaling in Development of the Cochlear Tonotopic Gradient

We all know how a piano works: the keys trip tiny hammers that in turn strike an array of strings. Mellifluous sounds then emerge when the strings vibrate in an orderly pattern. In order for us to enjoy these complex sounds, our sense of hearing must perform the opposite operation: it must decompose every sound we hear into its pure tonal components. The ear accomplishes this feat by several means, using both mechanical and electrical strategies. The key point, though, is that the ear possesses a row of tiny tone detectors, each tuned to a specific frequency of sound. At one end of this array, these cells sense the lowest bass note; at the other, they respond to the highest alto trill. Unlike the strings of a piano, which can produce 88 distinct notes, our hearing organs can detect over 4,000 different tones. The question arises, then, how do our ears develop the capacity to resolve these tones? Who tunes the thousands of strings in the ear's piano?

Łukasz Kowalik has asked this question by studying the biochemical properties of cells along the sensory organ in the chicken's ear. He compared the genes expressed by low-frequency receptor cells to those in high-frequency cells and found dozens of genes with strikingly different patterns. Most importantly, several of these are genes known to participate in the patterning of biological structures. Indeed, when Łukasz interfered with the expression of these particular genes, he was able to alter the properties of the ear's tone detectors. This suggests that the genes are involved in tuning our hearing organs and sets the stage for learning how.

Łukasz was born and raised in Poland, from which his parents have journeyed to be here today. He received his Bachelor's and Master's degrees from Trinity College at Cambridge University, where he excelled in chemistry. Along the way, he received recognition for his work from the Polish Chemistry Olympiad and from International Chemistry Olympiads in Montreal, Melbourne and Bangkok. Looking at Łukasz, it is not entirely clear how he got into the Olympics, but maybe chemistry has different requirements than track and field. Here at Rockefeller he has not only done fine research, but also played an important role in service to others by working for the Summer Undergraduate Research Fellows' program, organizing the university's film program and tutoring younger students. For my colleagues and myself, it has been a pleasure to work with Łukasz.

Young Nam Lee

presented by Paul Bieniasz

B.S., Furman University
Reconstitution and Characterization of Human Endogenous Retrovirus-K

Today is a special day for me. I have the honor of presenting the very first group of students to graduate from my laboratory.

The first of those is, in fact, the first student to have joined my lab, Young Nam Lee. For her Ph.D. Nam chose to become one of the very first scientists in an emerging field called paleovirology. Retroviruses can occasionally infect and integrate their genomes into the DNA of cells that later become sperm or egg cells. In so doing, they can be inherited, just like normal host genes, and thus become so-called endogenous retroviruses. This has happened on very many occasions through evolutionary time and consequently there is, in effect, a fossil record of ancient, extinct retroviruses in the genomes of modern organisms. About eight percent of your DNA is composed of old, dead retroviruses.

Nam made several discoveries in the lab, but her key achievement was to show that it is possible to resurrect extinct endogenous retroviruses. In particular, using multiple defective endogenous copies as a guide, she synthesized, from scratch, an infectious form of an extinct retrovirus that infected the ancestors of modern humans for many millions of years and is fossilized in the genomes of each of us. Nam's groundbreaking achievement allowed her, and others that followed, for the first time to study numerous aspects of the biology of extinct viruses. This piece of work really ignited the field of paleovirology, inspiring many others to follow Nam's lead.

I was very fortunate to have Nam as my first student. She had all the attributes one could hope for in a young scientist. But what I will remember most about Nam is her fiercely independent, pioneering spirit and her remarkable drive and commitment to get projects going and make them work. I will remember the occasional tears when things weren't going well, but I'll remember them fondly because they were what told me what was particularly special about Nam, namely how extraordinarily deeply she cared about the work. That shared commitment to discovery, and the success that ensued, made my first experience of mentoring a Ph.D. student an especially rewarding one. Nam completed her thesis and left the lab almost a year ago to become a postdoctoral fellow with Anita Sil at UCSF. Knowing what I know about Nam, I'm certain that further successes will shortly follow.

Bluma Jessica Lesch*

presented by Michael W. Young on behalf of Cori Bargmann

B.S., Yale University
Mechanisms for Maintaining Cell Identity in Caenorhabditis elegans
Olfactory Neurons

The right and left sides of our brains are different. Each of us has a preferred right or left hand, and only one side of the brain, usually the left, can generate language. Bluma Lesch — Bibi — came to the Tri-Institutional M.D.–Ph.D. program from California by way of Yale. Thinking, perhaps, of the left and right coasts, she has asked how the asymmetric brain develops and persists through life.

A transient early signal triggers a left-right asymmetry in the brain of *C. elegans* that is maintained long after the signal disappears. Bibi identified two transcriptional regulators that capture and propagate the transient signal. One transcription factor, nsy-7 (pronounced "nosy"), acts early in life to transform the unstable developmental signal into a long-lasting cell fate. The second transcription factor, a conserved homeodomain protein called hmbx-1, acts much later in life to maintain neuronal properties. Young animals with hmbx-1 mutations are normal, but in adults, specific neuronal markers and brain asymmetry are lost.

Especially early in life, the brain changes through experience. Bibi showed that neuronal activity supplements nsy-7 and hmbx-1 by regulating overlapping promoters, reinforcing and modifying the developmental pathways for brain asymmetry.

Autism, schizophrenia and epilepsy are disorders in which the early development of the brain is normal, but neuronal properties become disordered later in life. This is exactly the process that Bibi has elucidated in her elegant thesis work, which shows how genes and the environment cooperate to shape the brain.

Ying Lu

presented by Frederick R. Cross

B.S., Peking University
Mitotic Exit Control in Budding Yeast: Regulators and Dynamics

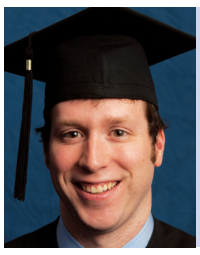
Ying Lu arrived at Rockefeller after undergraduate work in China, in physics. I gather that he was very well versed in physics — although I can't judge this for myself, he won the International Physics Olympiad, where I assume they ask you some hard questions.

He started work in my lab with no exposure to experimental biology at all, but learned to carry out all the procedures in the lab in a very short time, then started to improve them, especially anything related to quantitative image analysis. At the same time, he rapidly developed his own strong scientific opinions about the system — his ideas were

frequently at odds with what people in the field thought, and frequently at odds with what I myself had believed. Ying's claims about how things worked seemed to come not just from left field, but from some whole different ballpark, one that I had never visited, but experience taught me that his point of view was always well worth exploring, and turned out to be correct a really unjustifiably high proportion of the time.

Ying's major accomplishment concerned analysis of regulation of subcellular localization of a phosphatase through the cell cycle. This sounds like a straightforward if challenging bit of cell biology to work out, but what actually happened was that Ying first found some utterly bizarre behavior in this system, and then simultaneously came up with a mechanistic explanation and a conceptual framework to explain the whole thing that constituted an entirely new idea of how cell cycle control works in general. He then obtained quantitative experimental evidence to support his new cell cycle theory, and got the whole thing prominently published, to great acclaim (and with my name on it, largely as a passenger).

If you think that this sounds like an implausible accomplishment for a Ph.D. thesis starting from almost zero biological background, I think so too, but these are the facts. Ying is now pursuing postdoctoral work with Marc Kirschner at Harvard — as far as I can tell, Ying mostly chose this lab because Marc is clever enough to let Ying do whatever he wants. I look forward to hearing the outcome.



Robert Kendall McGinty*

presented by Tom W. Muir

B.S., Iowa State University

Mechanistic Insights into the Stimulation of Dot1L-mediated Methylation of Histone H3 by Semisynthetically Ubiquitylated Histone H2B

Rob McGinty joined the Tri-Institutional M.D.-Ph.D. program in the fall of 2002. After his initial medical training, his interests in protein chemistry led him to join my research group for his Ph.D. studies. I was happy to accept Rob for two reasons. Firstly, as an undergraduate at Iowa State he had carried out very nice research in the area of protein NMR, suggesting an aptitude for research. Secondly, he had been a collegiate level swimmer, which I hoped would provide him with the strength, stamina and, importantly, love of water, needed for a successful tour of duty in my lab.

Rob was an amazing student, one of the very best I have ever graduated. He is the consummate chemical biologist. While some students trained in this area might be viewed as being neither fish nor fowl, Rob produced a body of work in my lab that is stunning from either the viewpoint of a chemist or, I would venture, a biologist — I guess his training as a swimmer prepared him to be both fish and waterfowl. Rob's Ph.D. thesis work began in the area of synthesis. At my suggestion, he took on the problem of how to synthesize proteins modified with the small protein ubiquitin — a very important biological target and by far the most daunting synthesis project my group had accepted. The challenge here was such that I seriously thought Rob would do well, in his thesis, if he simply helped establish a base camp en route to an eventual successful synthesis. In fact, it took Rob a little over two years to develop a general synthesis of ubiquitylated proteins — one that blended classical organic chemistry, photochemistry, peptide chemistry and protein chemistry.

In terms of organic synthesis, this work represents the high-water mark for my lab. It is a beautiful piece of work, highlighted by some truly lovely chemistry, which needless to say was aqueous-based. Most students might have hung up their speedos at this point, but not Rob, rather he used this as a bridgehead for the next phase of his work, namely to study the role of ubiquitylation in the area of chromatin biology. For this, Rob had to prepare chemically defined chromatin containing the ubiquitin modification, the biggest complex we have ever made. He then used this to show the ubiquitylation mark in one of the histone building blocks of chromatin is sufficient to stimulate lysine methylation in another histone — this was the first demonstration of direct biochemical crosstalk between two histone posttranslational modifications. Rob subsequently went on to tease apart the underlying mechanisms of this crosstalk by performing the first full enzymology study of a methyltransferase enzyme on a chromatin substrate. Rob was insanely productive during his Ph.D., authoring eight papers and counting. As important, he has made the critical contributions that have led to a major new research direction in my group, namely in the area of epigenetic mechanisms.

Rob was not only a leader in the lab, but also acted as "the skipper" in many a lab trip, which curiously always seemed to involve some kind of water activity. Few in my lab will forget his formidable navigation skills during a kayaking trip in Long Island where a supposed waterfall he had spotted far off in the distance turned out to be an open sewage pipe when we got there. Still, things could have been worse, since it turns out that the other passion he picked up while in Iowa, besides swimming and water sports, was watching hog racing. I have no idea what this is, but I don't think it happens in the Upper East Side. Rob has now returned to the wards to finish off his medical training, and we certainly wish him all success for the future.

Justin N. McManus

presented by Charles D. Gilbert

B.S., Cornell University

Dynamic and Integrative Properties of the Primary Visual Cortex

Justin McManus worked on the mammalian visual system, where he showed how neurons change their function in the long term, as we assimilate new experiences, and in the short term, as we interpret our surroundings. In this work he has made important contributions toward our understanding of the mechanism of information processing by the brain. These discoveries, though focused on the visual cortex, are relevant to the function of all areas of the cerebral cortex. Each area represents, in its circuitry, a set of potential associations between the elements that comprise our experiences. In the visual cortex a field of associations underlies our ability to link the components of visual scenes into complete objects, and to segment objects from their background. Justin showed that these associations are subject to top-down influences. When animals perform different perceptual tasks, the effectiveness of connections within the cortical circuit is changed so that individual neurons can assume different functions. These findings will change our view of cortical function from the classical notion whereby each cortical area has a fixed, stereotyped function to one where it is seen as a dynamic, adaptive processor, such that neurons can selectively express subsets of their inputs to execute different calculations.

Justin's contributions extended the idea of an association field that can be dynamically expressed on a moment-to-moment basis to make a model of functional recovery following damage of the central nervous system. His model showed how vision can be optimized in people suffering from adult macular degeneration, the most common form of blindness in adults. Based on findings of the remapping of cortical topography following retinal lesions, the model demonstrated that cortical plasticity can enable the visual system to fill in the gaps in images caused by retinal damage. This model, which he is now testing experimentally, will aid in future work designed to promote functional recovery following stroke and neurodegenerative disease.

In all his work Justin has shown extraordinary breadth in applying a range of experimental and theoretical approaches. He is a skilled physiologist, recording the activity of neurons in behaving animals. He brings sophisticated expertise in applying complex statistical analyses of the response properties of neuronal populations. He uses computational models that provide the link between electrophysiological studies and perception. And in his spare time he has contributed to the projects of other members of the laboratory, by fabricating new instrumentation, programming computational tools and developing data analysis. I look forward to seeing the new discoveries that will come from his ample bag of tricks in the future.

Melinda Miller

presented by Bruce S. McEwen

B.S., New York University

Structural and Molecular Correlates of Individual Differences in Anxiety Behavior and the Response to Stress

Melinda Miller graduated from NYU in behavioral sciences in 2003 and joined our laboratory in 2004 to study brain mechanisms of fear and anxiety. At NYU she had been part of studies of human fear learning with Professors Elizabeth Phelps and Joseph Ledoux. Fear learning involves a brain structure, the amygdala, as well as other brain regions, such as the prefrontal cortex and hippocampus, that are involved in emotional control and also in contextual memory, that is, remembering where you were and what you were doing when something important happened.

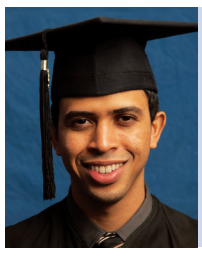
Melinda's experience with human subjects created a curiosity about underlying brain mechanisms, and she joined our laboratory to investigate an animal model of post-traumatic stress disorder (PTSD). She felt that animal models would give more information about mechanisms. Little did she know what she was in for! Nevertheless, with cleverness and persistence, she did indeed uncover novel and interesting mechanisms that may turn out to be more important than her original goal.

What Melinda discovered was that laboratory rats, while being quite homogeneous genetically, nevertheless differ considerably as far as baseline anxiety and also how they react to chronic or traumatic stress. Melinda measured anxiety by unwillingness of the animal to explore a brightly lit open area and she also measured the size of neurons in the prefrontal cortex (PFC), a brain region that inhibits the anxiety response. She found the more anxious rats had a smaller dendritic tree and thus the PFC may have been less able to do its job. The dendritic tree is the part of a neuron that receives synaptic connections from other nerve cells.

Melinda then delivered chronic stress by restraining the rats daily for three weeks and she delivered acute, traumatic stress by exposing rats once, while restrained, to the odor of a cat, a natural predator. Besides causing those prefrontal cortex neuron dendrites to shrink further, Melinda found that stress caused a neurochemical called CART to be increased by both chronic and traumatic stress in several brain regions, but only of those animals that were resilient or resistant to the stress, that is, that did not show further increases in anxiety. Those resilient rats were some of the animals that had low levels of anxiety to begin with.

Although these complexities of individual differences and resilience to stress diverted Melinda from her original path, her imagination, keen observation of behavior, as well as technical skill in molecular and anatomical methods, led to a novel and very interesting set of findings. One can tell the character of someone best under adversity and Melinda showed not only optimism but also a remarkable persistence and resilience. She succeeded, as they say, in "making lemonade out of lemons." Melinda is also a food connoisseur and a phenomenal baker of sweet things, and she did exactly that, making lemon squares out of lemons for the lab and members of her thesis committee.

We congratulate Melinda and also recognize and salute her parents, Rhonda and Mitchell, her sister, Beth, and Melinda's husband, Lee, who should all be very proud of Melinda's achievements.



Kevin Mohammed

presented by Mark Muesing

B.S., Morehouse College

Dissecting the Contribution of the Carboxyl-terminal Domain and Tail of HIV-1 Integrase to Viral Dynamics and Enzymatic Function

Kevin Mohammed came to the United States from Tunapuna, Trinidad in 1999 as a student at Morehouse College in Atlanta, where he graduated *summa cum laude* in biology. Kevin comes from a family of science educators. His father was an outstanding teacher of chemistry and his older brother, Hamish, a doctoral epidemiologist. Hamish, his sister Tracey and Kevin's mother Janet are together on this day traveling from the Caribbean islands of St. Kitts and Trinidad to see Kevin receive his high honor.

Kevin came to Rockefeller University in 2003 and started in our lab in 2004. There, through diligent hard work and determination he completed a study of the function and utility of the extreme carboxyl-terminus of the HIV-1 integrase protein, an enigmatic region of that viral protein which is required by HIV-1 for its irreversible establishment within the infected cell. His thesis, *Dissecting the Contribution of the Carboxyl-Terminal Domain and Tail of HIV-1 Integrase to Viral Dynamics and Enzymatic Function*, a.k.a., "The Tail of Integrase is Only the Beginning of the Tale," has provided new insights into the protein's role in both integration and the precision of viral particle formation.

As Kevin grew up just north of the equator at 10 degrees latitude, here at 40 degrees north it took some time for him to accommodate to the colder winter months. However, in time, he did adjust, managing to travel downtown by bicycle to the Aaron Diamond AIDS Research Center on most days. Another consequence of his recruitment to the lab was the language barrier that first existed between us. Although Kevin speaks with the beautiful dialect of his island nation it was sometimes hard for us to communicate. For example, he once asked if I knew where he could get a "bear." I told him, "Bears? There are no bears in New York City." "No," he said, changing his tone, a "beer."

Kevin is certainly "a diamond in the rough" and going forward will proudly represent the university as a first-class scientist. I am reminded that the acronym for his country, Trinidad and Tobago, is TNT. And that's what Kevin is — pure dynamite.

Aaron Nagiel*

presented by A. James Hudspeth

A.B., Harvard College

Synaptic Specificity in the Zebrafish Lateral Line

One of the principal problems confronting the discipline of neuroscience is how the brain gets put together. Our brain contains something like 10 billion nerve cells, or neurons. Each of these makes an average of a thousand connections, or synapses, so there are about 10 trillion synapses between nerve cells. Obviously enough, there is nowhere nearly enough genetic information to specify each and every connection. Instead, there must be general rules that broadly instruct the neurons, then leave it to each of them to play out its specific program. What, then, are these rules?

To get at problems such as this, researchers like to use so-called model systems: simple examples of complex phenomena that lend themselves to laboratory investigation. This is why we know so much about bacteria, yeasts and fruit flies, and why those particular organisms have taught us so much about ourselves. Aaron Nagiel sought to identify the basis of specifying nerve connections in such a model system, the ordinary dime store zebrafish. This species can be raised easily in large numbers and is easy to work with. Moreover, its genes are much like our own — it has a backbone and the same set of internal organs as we — so what we learn from the zebrafish is generally applicable to our own species as well.

In brief, Aaron used an elegant set of genetic and molecular-biological strategies to demonstrate that nerve fibers grow to their appropriate targets by the use of chemical cues. More importantly, the cues in this instance may be related to the chemical signals that specify the body axes — that tell us which end of the body is the head and which the tail. Other researchers in our group and elsewhere are now seeking to amplify on this work and in particular to identify the specific signals involved.

Aaron joined us after studying at Harvard College, where he received a number of scholarships and awards for superior academic performance. Since completing his doctoral research, he has returned to medical school to complete his combined M.D.-Ph.D. training. Thereafter Aaron will find himself torn between research and clinical practice, quite possibility in ophthalmology. In the interim, he and his wife Svetlana have produced an elegant baby daughter who is now teaching Aaron a great deal more about neural development.

Johanna Napetschnig

presented by Günter Blobel

M.S., University of Vienna

A One Way Ticket to the Cytoplasm: Structural and Biochemical Analysis of Nup214 and Its Role in mRNA Export

Johanna grew up in the city of Klagenfurt in the southeastern corner of Austria. After graduating with a master's degree in genetics from the University of Vienna, Johanna moved to San Francisco, where she worked in the laboratory of a previous Rockefeller University graduate, Peter Walter. Her contributions there were recognized by a coauthorship in a very influential *Nature* paper that solved the crystallographic structure of two GTPases: the two G proteins of the signal recognition particle (SRP) and of its cognate receptor (SRP receptor) form twinning GTPases, stimulating each other's GTPase activity. Both of these molecular complexes are involved in the targeting of proteins for translocation across the prokaryotic plasma membrane and the eukaryotic endoplasmic reticulum.

In 2004, Johanna was accepted as a graduate student to Rockefeller and in the same year joined our lab. Again, her achievements here were spectacular. Together with André Hoelz, an assistant professor in our laboratory, she solved the crystal structure of the ADP form of an RNA helicase, Ddx19, bound to the β propeller of the nucleoporin Nup214, the crystal structure of which Johanna had published in an earlier paper. At about the same time, the crystal structure of the ATP form of Ddx19 helicase in association with a short RNA segment was reported by another laboratory. Together these data allowed reconstruction of how consecutive ATPase cycles of the helicase strip the numerous nuclear mRNA binding proteins, one by one, from mRNA, as it emerges, 5' end first, at the cytoplasmic side of the nuclear pore complex. Johanna's structure revealed that the large and highly conserved basic surface of the ADP helicase interacts with a highly conserved acidic surface of the β propeller of Nup214 which is located at the cytoplasmic side of the nuclear pore complex. Upon ADP/ATP exchange, the ATP helicase dissociates from Nup214, making the basic surface of the helicase available to compete with the basic surface of an mRNA binding protein and thereby displacing the mRNA binding protein and binding directly to mRNA.

Johanna will continue her work in structural biology across the street and join Dr. Wu's laboratory at Cornell as a postdoctoral fellow.

John T.G. Pena*

presented by Thomas Tuschl on behalf of himself and Charles D. Gilbert

B.S., B.A., Oakland University

Localization and Function of RNA Interference in the Cerebral Cortex

It is my great pleasure to present John Pena. John participated in the Cornell/Rockefeller M.D.-Ph.D. program and joined two laboratories, Charles Gilbert's, and mine, the Tuschl lab. John developed methods to manipulate and study the RNA interference pathway in neuronal tissues. For Dr. Gilbert, he engineered viruses to deliver double-stranded RNA to nerve cells. The virally expressed dsRNAs were used by RNA interference machinery to direct the silencing of specific genes and thereby study their function. In my laboratory, John developed a novel approach to visualize microRNAs, the small RNAs that naturally occupy the RNA interference machinery, in brain tissue sections.

His studies not only led to important publications but also to a patent application. This commercial aspect of his invention inspired him to continuously suggest business plans and new and bigger revenue-generating research ideas. His most successful early business schemes involved one-dollar bets with his heads of labs on seemingly impossible research goals. These dollar bills were then displayed prominently over his research desk, to remind me and his colleagues that for John, everything is possible.

I wish to John that he continues to succeed in turning his visions into reality.

Assaf Raz

presented by Vincent A. Fischetti

B.Sc., Tel Aviv University

Regulation of Surface Protein Assembly on the Wall of Gram-positive Bacteria

After a bacteriophage enters the cell its nucleic acid takes over the cell for the production of new virus particles. Within about an hour, the cell is filled with as many as 100 viruses. The problem now faced by the phage is how to get out of the cell. They solve this problem by producing an enzyme that will degrade the bacteria's cell wall causing the bacteria to explode, releasing the progeny phage.

Assaf Raz came from Israel and was interested in working on surface proteins on gram-positive bacteria. Surface proteins are critical for bacteria to cause infection. Most disease organisms could have up to 10 or more different surface molecules and thousands of copies of each — sort of like the fuzz on a tennis ball. Since naked bacteria cannot cause infection, information on how these molecules are placed on the bacterial surface would allow possible intervention and control of these disease bacteria. The problem that Assaf faced was that the cell wall of gram-positive bacteria is impermeable to reagents such as specific antibodies that he could use as probes to examine the cell's interior.

Assaf solved the problem by employing the same enzyme that the phage uses to get out of the cell. He used this enzyme to drill holes in the cell wall allowing his reagents to penetrate into the cell. His studies were pioneering in that for the first time scientists could probe the interior of gram-positive bacteria to perform cell biology experiments.

Using this method, Assaf found that the molecules responsible for surface protein assembly were found in foci that migrated from the newly growing septum to the polls of the cell. He found that in the absence of these molecules, the surface proteins became jammed in the bacterial membrane and were lethal to the cell. This observation could be the target for a new type of anti-infective.

When he is not looking into cells Assaf loves to hike and will make every effort to be in the outdoors. A far cry from his previous hobby — a tank driver in the Israeli army.

Assaf will stay on in the lab to complete many of the projects he has initiated.

Joshua J. Riegelhaupt

presented by Jan L. Breslow

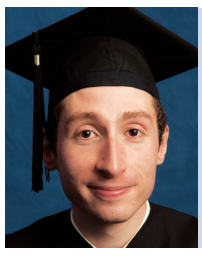
S.B., Massachusetts Institute of Technology

Characterization of the Functional Role of StARD4 *in Vivo and Investigation of Epigenetic Modulation of* ApoA-I *Transcription*

It is my pleasure to introduce Josh Riegelhaupt upon the occasion of his graduation. Josh grew up in Manhattan, but made the pilgrimage to Boston for college, receiving his undergraduate degree from MIT. After deferring entry for a year of travel, Josh entered the Rockefeller graduate program in the fall of 2005.

In the summer of 2006 Josh did a rotation in my lab and I assigned him the task of creating a knockout construct for a gene named *StARD4*. He accomplished this with the help of Marc Waase, an M.D.-Ph.D. student in our lab at the time. *StARD4* is an intracellular cholesterol transport protein that contains a START domain, one of 15 such proteins and genes in mammals. This protein/gene had been discovered a few years prior by another student, Ray Soccio, as a liver gene regulated by dietary cholesterol, but its precise function was still unknown. After his rotation Josh returned to do his Ph.D. thesis, and the two projects he initially focused on were obtaining a *StARD4* knockout mouse, and a new project studying the epigenetic regulation of transcription of the gene for the major HDL protein, apoA-I. Although he made some progress with the latter, once he got the *StARD4* knockout mouse he chose to focus on its characterization, and phased out the apoA-I project. Josh was able to document several metabolic abnormalities in the *StARD4* knockout mouse, and now that he is leaving the project is being continued by a postdoc, Jeanne Garbarino, using Josh's mice as well as in vitro cell culture approaches. Ultimately, we hope this project will teach us something fundamental about intracellular cholesterol transport and how it affects metabolic pathways.

Josh is very smart and, as important, he is dogged. If something is not working, Josh takes apart the problem and no matter what the investment of time and effort he sticks with it until it is solved. Over the past four years I have watched Josh's science mature, but also watched him mature as a person. He has become much more comfortable with his identity and direction in life. After graduation he is exploring opportunities in biotech startups, and I am sure he will be very successful.



Jonathan A. Robbins*

presented by Frederick R. Cross

B.A., University of Pennsylvania

Regulation of Anaphase Promoting Complex Coactivators

Jon Robbins came to my lab from the M.D.-Ph.D. program to learn about the cell cycle. The anaphase promoting complex (APC) is a central cell-cycle regulatory component, controlling degradation of many proteins, so its regulation is quite important. This problem had received a lot of attention previously, but the previous work seemed qualitative and imprecise, and we thought that an accurate evaluation of the importance of different kinds of APC regulation would be valuable. Jon took on this topic with admirable vigor and enthusiasm, and was able to provide clear and definitive evidence for popular ideas, such as critical regulation of APC by phosphorylation, that had never before been tested rigorously.

Of course, finding compelling evidence for things that people already believe does not provoke much controversy, although it's much more important than people tend to realize. However, Jon continued to carry out very accurate and complete experiments, and soon found that some other popular ideas in the literature were not so well supported; in fact, they were completely wrong. A known function of the APC is to block formation of the mitotic spindle until after cell cycle initiation. Jon's work demolished the one claim in the literature for how this happens (a moderately appealing but fundamentally unsupported hypothesis), and Jon's work also provided a very interesting alternative view — his careful quantitative measurements, carried out at physiologically meaningful levels of all components, allowed him to place different modes of APC regulation in the context of overall cell- cycle control. Along the way, Jon was obliged to demolish some favored ideas of his own that early experiments had supported, but that did not stand up to the very thought-

ful, careful and critical analysis that was Jon's experimental style.

Jon is now back in medical school, and seems very busy for some reason — he does come around periodically to talk about his medical training, which he seems to be going through with the same care and critical acumen that characterized his graduate work. Jon looks to be a sure bet for becoming a terrific physician-researcher — he is both an accomplished and critical scientist and an empathetic and caring person. I look forward to seeing where Jon takes his abilities and interests in the years to come.

Brad R. Rosenberg*

presented by F. Nina Papavasiliou on behalf of herself and Charles M. Rice

B.S., M.S., Yale University
Identification and Characterization of APOBEC1 *mRNA Editing Targets: A Transcriptomics Approach*

It's my great, great pleasure today to introduce Brad Rosenberg.

Brad came to the lab four a half years ago, on a quest to understand what a neglected deaminase, a molecule called APOBEC1, was up to. What was known at the time was that this enzyme catalyzed a mutation in a particular mRNA, which resulted in the truncation of a molecule called apoB, which is important in lipid metabolism.

APOBEC1 was in fact discovered as the mutator for apoB. And this is the way all of the enzymes of this family have been discovered: first, you have the phenotype, and then you identify the protein machinery that does it. Brad decided to go the other way around. He started from the enzyme, and set forth to identify all the possible targets, and to then understand the phenotypes associated with those new targets. And this is really the proverbial needle-in-a-haystack experiment, that prompted one of our colleagues to say to Brad "you are a really brave young man!"

Brad is certainly brave but also persistent, brilliant, unfailingly upbeat and with the mark of a true scientist: he just does what needs to be done, learns what needs to be learned, to make things work. So, true to form, Brad succeeded brilliantly in identifying and validating a number of specific needles, or mutations, in the haystack that is the entire transcriptome of a cell. He has also begun to understand what these mutations do: some of them at least appear to erase binding sites for small RNAs that regulate protein translation.

If I were then to summarize Brad's Ph.D. research, I'd say that he has taken a neglected enzyme and discovered how it modulates a completely new pathway of gene regulation. He has therefore generated a new field of research, as well as new tools that many folks around here now use. (Which is why Brad is extremely popular amongst us!)

We'll miss him dearly, as he goes back to medical school to complete his dual degree.

Yasunori Saheki

presented by Sidney Strickland on behalf of Cori Bargmann

M.D., Okayama University Medical School
Mechanisms of Presynaptic CaV2 Calcium Channel Localization in Caenorhabditis elegans

Yasunori Saheki came to Rockefeller from Kobe, Japan. His grandfather was a renowned amateur astronomer — a crater on Mars is named Saheki. Where his grandfather wielded a telescope, Yasunori wielded a microscope to answer a fundamental question about how neurons function.

Synapses are the sites where electrical signals in neurons are converted to chemical signals between neurons. Yasunori examined a key molecule at the synapse, the voltage-activated calcium channel, which detects electrical changes to allow calcium into the presynaptic cell; calcium then triggers neurotransmitter release onto postsynaptic cells.

Yasunori asked: How do calcium channels get to the synapse, shunning all other parts of the cell? He tagged the massive alpha1 subunit of the channel with green fluorescent protein, allowing him to see the individual synapses where the channel resides. He then carried out a screen for mutants whose calcium channels were abnormally localized. He discovered the *calf-1* gene, which is necessary for the calcium channels to leave their site of synthesis in the endoplasmic reticulum. Through studies of *calf-1*, the calcium channel and its accessory subunits, he showed that *calf-1* mobilizes fully active calcium channels for exit from the endoplasmic reticulum, coupling channel traffic with functional maturation.

Yasunori's discoveries about *calf-1* and two other genes have provided new insights into channel traffic between internal compartments and the cell surface. This is an important question, as channel traffic is implicated in learning, and is the target of clinically relevant drugs.

Daniel Schmidt

presented by Roderick MacKinnon

Diplom, University of Tübingen
Lipid Chemistry and Mechanical State of the Membrane Modulate Ion Channel Function

I'm proud to introduce Daniel Schmidt. Daniel carried out a fundamental and important work for his Ph.D. thesis. His project, quite separate from the mainstream efforts of our lab, reflects his independent approach to life and science. Most of us in the field of membrane protein structure and function have implicitly assumed that the cell membrane is an inert coat into which the membrane proteins are plugged, and these proteins give rise to all the interesting properties of the cell membrane. In a series of very important papers, Daniel showed that the lipid membrane plays an essential role in shaping the functional properties of ion channel proteins. He showed the different chemical features of the lipid molecules within a membrane control the rates at which the ion channels open, close and inactivate to tune the electrical properties of living cells. He also showed that certain ion channels are very sensitive to the mechanical stress on the cell membrane, and he's put forth a new quantitative theory for how mechanical sensation, for example touch, may be mediated by the same ion channels that normally produce the electrical impulses in our nerve cells.

Daniel is an engineer at heart. When it comes to building complicated experimental devices, he's a genius. He is an intuitive thinker and he thinks deeply and clearly. He has the potential for great discoveries and I look forward to following his career in science. Behind intense eyes, Daniel is a kind and gentle person who never hesitates to spend his time helping others. He has helped me enormously, often pointing out ways in which we could make our lab a better place, simply because he cares. I, and everyone in our lab, will miss him dearly.

Steven Joseph Soll

presented by Paul Bieniasz

B.S., Portland State University
The Impact of Host Factors on Retroviral Evolution and the Identification of a Novel Receptor That Was Used by an Ancient Primate Retrovirus

When Steven Soll joined the lab it was clear that he had a strong interest in evolutionary biology. Thus it was natural that he also became a pioneer paleovirologist. Steven worked on two particular groups of extinct retroviruses that infected very many of our ape and monkey relatives over the past few million years. He asked why human ancestors were apparently protected from infection by these retroviruses and why these retroviruses became extinct. In so doing, and using a resurrection approach, he became the first to identify a receptor for a virus that is not only extinct, but for which no functional viral genes existed. Additionally, working with David Perez-Caballero, Steven showed that many of these fossilized viruses met their end via encounters with specific cytidine deaminases that are recently-discovered components of the innate immune system. These cytidine deaminases can cause hypermutation of retroviral genomes and, in additional studies that are ongoing, Steven has also explored how they affect the fitness and evolution of viral populations in a modern retrovirus, namely the AIDS virus, HIV-1.

Steven is a remarkable individual. He is endowed with an especially powerful brain, which he uses to great effect as a scientist. He thinks incredibly deeply about his experiments, about how to design them and what they mean. He is as critical of his own data as he is of others', an important attribute for a scientist. Steven is also exceedingly generous and genial, he loves to talk about science and he is a real pleasure to know. He has told me that he has an urge to teach; I can absolutely see in his character why this is the case. He also has an interest in music, and a few of you may have been fortunate enough to catch a Steven Soll performance in one of New York's bars over the past couple of years. So I'm not sure whether Dr. Steven Soll is going to be a scientist, a teacher or rock star. Whatever path he chooses to follow, I know he will be terrifically good at it.

Boo Shan Tseng

presented by Hironori Funabiki

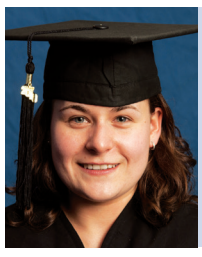
S.B., Massachusetts Institute of Technology
Regulation of Chromosome Segregation by the Chromosomal Passenger Complex

Boo Shan Tseng, born in Hong Kong, grew up in New York since she was two, first in Brooklyn and Queens and then in upstate New York, Plattsburgh. After graduating from MIT, Boo came back to New York to enroll in the graduate program at Rockefeller, and chose to join my laboratory to study mitosis, one of the most fundamental events in life.

Mitosis is a festival of the cell cycle — chromosomes take off ordinary proteins and put on special ones to perform a well-organized dance. Boo first asked how chromosomes can change their clothes during mitosis, without affecting genetic or epigenetic information of chromosomes, and through collaboration with David Allis, she made a key contribution to the field by revealing that a specific histone phosphorylation plays an important role. Boo next attacked a problem of how chromosomes can create their own dancing hall, namely the bipolar spindle, which is made of dynamic polymers, microtubules. Chromosomes are not just shyly waiting for microtubules to visit, but they actively emit signals to induce microtubule assembly. After years of painstaking trials, Boo discovered that the kinase Aurora B must detect both chromosomes and microtubules to build up the spindle. This dual-detection mechanism helped to explain why the spindle is made only around chromosomes. This work will be coming out in *Developmental Cell* next week.

Like a chromosome, Boo is extremely organized, but at the same time, energetic and highly active. She was able to accomplish a complex series of experiments by meticulously planning using her self-styled worksheets, and by diligently recording precisely what she has done and observed. Her talkativeness contributed to lively discussions during lab meetings and to the cheerful atmosphere of the lab. I will certainly miss her big smile, as well as many birthday cakes that she supplied to us for last several years.

After finishing up a couple more projects, Boo will join Matthew Parsek's group at the University of Washington to characterize the composition and function of biofilms formed by bacteria. I'm sure that Boo will bring an order and brightness to Seattle, while contributing to the understanding of the molecular basis for bacterial infection.



Maria Zhadina

presented by Paul Bieniasz

B.S., Brandeis University
Role of Ubiquitin Ligases in Retroviral Budding

During her time in my lab, Maria Zhadina showed how a small protein called ubiquitin is employed to enable the release of certain enveloped viruses as they bud through the membrane of infected cells. This had been very enigmatic area, since the discovery, by my lab and others, some years ago, that two sets of cellular machinery are required for this process. One is the so-called ESCRT machinery, which has membrane scission activity, and the other is a family of enzymes that attach ubiquitin to other proteins. In an elegant set of experiments, Maria made the counterintuitive finding that the actual identity of the protein to which ubiquitin becomes attached during viral budding, be it viral or cellular, is unimportant. Rather, she showed that the mere proximity of ubiquitin to the site of particle assembly, and crucially, its ability to actually bind to and recruit specific components of the membrane scission machinery, are key to completing the genesis of new viral particles.

Maria worked with a retrovirus that has special advantages for this particular series of studies but is actually a rather difficult virus to work with. Fortunately, the difficulties of the experimental system were not evident in Maria's work. That's because of Maria's unique gift — she is unquestionably the most adept experimentalist I have ever encountered. She makes experiments work beautifully that others struggle with. There are some pretty formidable scientists in this room but I doubt that any have skills at the laboratory bench that exceed those of Maria. Her sheer ability, along with heavy doses patience and determination, allowed Maria to arrive at insights that would be beyond the abilities of most others. Maria is going on to Cornell Medical School. I don't know what the future holds for her, but if she insists on not returning to basic science, I would recommend brain surgery or some similar discipline as an appropriate specialty for someone of her quite remarkable skills.