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The Rockefeller University

SCIENCE FOR THE BENEFIT OF HUMANITY

BENCHMARKS

THE COMMUNITY NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

FRIDAY, JULY 13, 2012

The 2012 Convocation honored one of the largest graduating classes in Rockefeller history with 40 Ph.Ds awarded, bringing the total number of Rockefeller alumni to 1,110. Celebrations included an evening reception for the graduates and their families, a luncheon, the traditional cap-and-gown procession across campus, a formal ceremony in Caspary Auditorium during which graduates were presented with personal remarks from their mentors and a campus-wide celebration on the Peggy Rockefeller Plaza. Members of the class of 2012 — 20 men and 20 women — come from fourteen countries: Argentina, Australia, Bolivia, Canada, China, France, Germany, Japan, Korea, Mexico, Nepal, Singapore, United Kingdom and the United States. Of the 35 students in the Ph.D. program, 22 will do postdocs, three will teach, three will work in law firms, two in consulting firms, two in industry and three are undecided. The five participants in the Tri-Institutional M.D.-Ph.D. program will return to medical school to finish their medical degrees.

This annual Convocation issue of BenchMarks *salutes the 2012 graduates of The David Rockefeller Graduate Program.*

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

BENCHMARKS

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PHOTOS: DARREN ORNITZ AND ZACH VEILLEUX

Honorary degree recipients advanced knowledge of RNA function

by LESLIE CHURCH

Two pioneers in the field of molecular biology were recipients of the honorary doctor of science degree at the June 14 Convocation ceremony: Rockefeller's own James E. Darnell Jr., Vincent Astor Professor Emeritus and head of the Laboratory of Molecular Cell Biology, and Yale University's Joan A. Steitz, Sterling Professor of Molecular Biophysics and Biochemistry and an investigator at the Howard Hughes Medical Institute.

The two scientists have made groundbreaking discoveries on RNA and how it is processed, contributing to our understanding of illnesses ranging from cancer to autoimmune diseases. In addition to their scientific influence, both Dr. Darnell and Dr. Steitz are renowned mentors and role models for younger scientists.

Dr. Darnell, who has been described as the "father" of RNA processing and cytokine signaling, received his M.D. in 1955 from the Washington University School of Medicine. After research at the National Institute of Allergy and Infectious Diseases and the Pasteur Institute in Paris, among other appointments, he joined Rockefeller as Vincent Astor Professor in 1974.

During his nearly six decade career, he made numerous discoveries in the cells of higher organisms that established the central role of RNA. In his later work, Dr. Darnell and his colleagues mapped the first complete "signal transduction" pathway: the JAK-STAT signaling pathway. He has received numerous awards, including the 2012 Albany Medical Center Prize in Medicine and Biomedical Research, the 2003 National Medal of Science and the 2002 Albert Lasker Award for Special Achievement in Medical Science.

From 1990 to 1991 Dr. Darnell served as vice president for academic affairs at Rockefeller and was instrumental in the 1980s and 1990s in establishing a new focus in hiring young independent faculty, a now accepted mechanism in university practice.

"Nothing matches the joy, indeed the exhilaration and the deep satisfaction, of being recognized by the home team," Dr. Darnell said in accepting the degree. He went on to call graduates to action in educating young people about science. "In this country we especially need to engage children, young students at all ages, far more actively than has been customary in the past. Please, put aside five percent of your time to whatever public school you choose. I can assure you your efforts are desperately needed."

PHOTO: DARREN ORNITZ

PHOTO: ZACH VEILLEUX

Honoris causa. Joan A. Steitz, top; James E. Darnell Jr., bottom.

Dr. Steitz was the sole woman in a class of 10 to begin graduate studies in biochemistry and molecular biology at Harvard in 1963, and the first female graduate student to work under Jim Watson's guidance. In the Watson lab, she became interested in bacteriophages and the question of how a ribosome recognizes the beginning of a gene for translation. After receiving her Ph.D. in 1967, Steitz did postdoctoral work at the Medical Research Council Laboratory of Molecular Biology in Cambridge, England, using early methods to determine RNA sequences that instruct ribosomes to initiate protein synthesis on bacterial mRNAs.

In 1970, Dr. Steitz joined the faculty at Yale where her laboratory discovered and defined the function of small nuclear ribonucleoproteins (snRNPs), cellular complexes which play a key role in the splicing of pre-messenger RNA. Her many honors include the 2008 Albany Medical Center Prize in Medicine and Biomedical Research, the 2006 Gairdner Foundation International Award and the 1986 National Medal of Science.

When accepting her degree, Dr. Steitz remarked on her experiences in the field of molecular biology and its evolution. "In the course of a single career, momentous changes have occurred both in science itself, and in who conducts the science. Your future in science holds many wonderful surprises and opportunities, along with, obviously, real challenges. It's important to have goals, to continue to do what you are passionate about, and it's important to enjoy what you are doing."

Daniel Gilmer awarded David Rockefeller Fellowship

by LESLIE CHURCH

Daniel Gilmer, a graduate fellow in Vincent A. Fischetti's lab, has been awarded the 2012 David Rockefeller Fellowship, given each year to an outstanding third-year student for demonstrating exceptional promise in science and leadership.

A native of Central Florida, Mr. Gilmer is studying something that first sparked his curiosity as a child during a visit to the family doctor. "He told me that he had to prescribe different antibiotics to me when I got sick, because bacteria were becoming resistant to the antibiotics he had previously prescribed," Mr. Gilmer says.

It stuck, and now, 20 years later, Mr. Gilmer is in the Laboratory of Bacterial Pathogenesis and Immunology, investigating bacteriophage lysins, a new source of antimicrobials that could replace antibiotics.

"It is incredibly rewarding to address an issue that puzzled me as a child," Mr. Gilmer says.

The phage lysins Mr. Gilmer studies target *Streptococcus suis*, a bacterium that mainly infects pigs, and can be passed to humans when they handle infected meat. The infection can lead to meningitis and other severe inflammatory responses in humans. Recently, Mr. Gilmer codiscovered a new phage lysin cloned from *S. suis* that proved to be active against several bacteria.

Mr. Gilmer says he was drawn to this research because of its translational nature — it provides a clear route to impact human health — and the ease with which he can explain it to a lay audience.

"I want my work to inspire science literacy and investigation among nonscientists. I have found that when nonscientists understand the idea behind my work, they inquire further. This increases their knowledge, and challenges me to think about my work from novel perspectives," says Mr. Gilmer.

After graduating summa cum laude with a bachelor's degree in biology from Howard University in 2008, Mr. Gilmer began conducting research as a Postbaccalaureate Fellow at the National Cancer Institute of NIH, where he studied a cancer-related membrane transporter.

In fact, much of his research experience prior to joining Rockefeller in 2009 was related to cancer, but Mr. Gilmer had interests in other areas of biology as well. He was drawn to the university in part because of the freedom students have to explore multiple labs and find the right fit. He also could see that the university gave its students the resources they needed, academically and personally, to do their best work.

"I felt that Rockefeller would support me as a student to an extent unmatched by any other institution, and that has been the case. With my wife also in graduate school, and a one-year-old baby at the Child and Family Center, Rockefeller has enabled me to remain focused on my work."

Mr. Gilmer still finds time to get away from the bench, though: he plays basketball with students at Weill Cornell and enjoys biking around the city, completing the Five Boro Bike Tour the last two years. He's also an active mentor. Currently he oversees an undergraduate student from Washington University in Seattle and a local high school student through the university's outreach programs, and is working with a friend in Boston to build a mentoring network for African-American undergraduates.

"It's a pleasure to have Daniel in the lab," says Dr. Fischetti. "He is a dedicated, hard-working young scientist, with a true feeling of responsibility to the community. He truly deserves this award."

PHOTO: ZACH VEILLEUX

Fellowship. Daniel Gilmer (center) with Vanessa Ruta and Marc Tessier-Lavigne. Dr. Ruta, a Rockefeller alumna and previous recipient of the David Rockefeller Fellowship, presented the award.

Coming soon, to The David Rockefeller Graduate Program

As the Rockefeller community says goodbye to the graduating class of 2012, a new group of talented students is set to join the campus in the fall. Approximately 700 applications of potential new students were received this year, and after much deliberation by the admissions committee, that list was narrowed down to 87 acceptances. Of those, 19 have enrolled in The David Rockefeller Graduate Program this fall and one has deferred admission until 2013.

The 2012 entering class includes eight men and 11 women from 10 countries: Argentina, Australia, Canada, China, Greece, Korea, Myanmar, Romania, Turkey and the United States. Their alma maters include: Bogazici University, Brown University, Cornell University, Goucher College, McGill University, Monash University, Mount Holyoke College, Peking University, Rutgers University, University of Athens, University of Buenos Aires, University of Chicago, University of Massachusetts, Amherst, University of Pittsburgh, University of Richmond, University of Texas at Austin, University of Ottawa and University of Washington.

Teaching awards honor Brivanlou and Fuchs

Ali H. Brivanlou (right), head of the Laboratory of Molecular Vertebrate Embryology, and Elaine Fuchs, head of the Laboratory of Mammalian Cell Biology and Development, were this year's recipients of Distinguished Teaching Awards. The awards were established in 2005 to recognize outstanding individual contributions to the university's educational environment, and include a plaque and a monetary gift. Chosen by a committee that includes the university's scientific executive officers, the awards are presented each year to one or two faculty members. Since 2009, Drs. Brivanlou and Fuchs have taught a highly successful stem cell course at Rockefeller, which they organized themselves out of their enthusiasm for the material and because they felt it was important instruction for the students. The weekly course is organized into two parts: a seminar series open to the Tri-Institutional community, and a graduate lecture taught by the awardees called Stem Cells in Tissue Morphogenesis and Cancer. The course covers basic principles of stem cells from self-renewal to tissue development, homeostasis, wound repair and cancer. The teaching awards are presented by the president each year during the Convocation luncheon (Dr. Fuchs was unable to attend).

PHOTO: DARREN ORNITZ

The 2012 Graduates

Following tradition, faculty mentors gave congratulatory tributes to this year's graduates. These are the transcripts of those speeches, as they were read on June 14. Students in the Tri-Institutional M.D.-Ph.D. Program are marked with an asterisk.

Pablo Ariel

presented by Timothy A. Ryan

Licenciado, Universidad de Buenos Aires
Exploring Synaptic Vesicle Exocytosis

Pablo Ariel was born in Buenos Aires and grew up in part in the Netherlands and in part in Saudi Arabia and returned to Buenos Aires for his college work. His Ph.D. work focused on trying to understand one of the most important building blocks in the brain: the synapse. Our brains have 10 trillion synapses and it is widely believed that many brain disorders come from or manifest in improper synaptic function. Remarkably, we still know quite little about how normal function of these synapses is achieved and what controls how well they work.

Pablo developed new tools to allow one to interrogate the function of individual synapses, providing a new paradigm for asking questions about what key molecular parts help control function. His work is having profound impact on how we do our science. There was the B.P. era, before Pablo, and the modern era, P.P. — post Pablo.

Pablo, I am guessing, was born a researcher, as his mind was always synthesizing ideas and trying to connect the dots. I am sure his love of this type of inquisition will carry him far, for as many of us here on the faculty know, it is the desire to answer scientific questions, and the joy we have in racking our brains over the puzzles biology presents, that is at the core of all great scientists.

Moritz Armbruster

presented by Timothy A. Ryan

B.S.E., The Cooper Union
Dissecting Synaptic Vesicle Endocytosis

Moritz Armbruster was born in Stuttgart, Germany, and moved to the desert in Tempe, Arizona, when he was seven years old. Coming from a mathematically inclined family, he moved to New York and studied electrical engineering at the Cooper Union before enrolling for a Ph.D. here.

Moritz tackled the problem of how synapses work. Synapses package their payload of chemical messages, the neurotransmitters, into small synaptic vesicles. One of the great challenges a synapse faces is that it has only about 100 of these vesicles, and once used to deliver the chemical message they must be rebuilt. Moritz pushed the state of the art in our abilities to follow this rebuilding process in real time, which helped him determine one of the key control points of how the rebuilding is regulated.

Moritz is a remarkable individual with a huge number of talents. There is literally nothing he could not master in the lab. One of his lab mates once said that he has "ice in his veins," as nothing seemed to perturb him when he did experiments. It was key to his success as things always go wrong in complex experiments, but Moritz always took the attitude that the problem must be solvable, and then proceeded to solve it. He is a true master experimentalist.

Claire Elizabeth Atkinson

presented by Sanford M. Simon

M. Biochem., Exeter College, University of Oxford
Structure and Organization of Nuclear Pore Proteins Studied by Fluorescence Polarization Microscopy

Today I present for
your consideration
The nucleus — also known as
Claire's preoccupation
It's there one's DNA
yields interpretation
To determine, who you are,
your gene's implementation

The membrane around it's
for discrimination
Which signals can enter
for communication
Pores do all the work of
this mechanization
Cargo passes only
with interrogation

Claire wanted to resolve
the organization
Of the pore proteins and
their orientation
Which could only be done
by quantification
of the angle of light
beam's polarization
This nuclear field lacks
standardization
Many models exist
for visualization
Claire's results just might lead
to "Claire-ification"
With models subjected
to falsification

Leading worthy colleagues
to edification
But they are not the kind
for capitulation
We expected there'd be
some reverberation

With these fears dancing in
her imagination
Claire started assembling
her instrumentation
She knew it'd be a tough,
hard investigation
Existing machines would
need modification
New technologies would
need verification
If she wanted a clear,
fair prognostication

After so many years
of anticipation,
Claire has survived both me and
her examination
Leaving with a degree
and grand dissertation
Soon Chicago will be
her accommodation
Mr. Carson, President,
my recommendation?
Claire Atkinson receive
our congratulation!

Lindsey Ann Baker

presented by C. David Allis

A.B., Harvard College
PHDs, Stress and Starvation: The Identification of a New Rpd3 Deacetylase Complex Involved in the Yeast Oxidative Stress and Metabolism Pathways

Some hobbies require certain personality traits; for example, someone with patience and perseverance. If the hobby of doing science demands these skills, Lindsey Baker is well prepared to pursue it. Lindsey went after her Ph.D. "hobby" by focusing her attention on PHD fingers in Lindsey's favorite model organism — *Baker's* yeast — of course. Lindsey turned her talents on a new histone deacetylase (HDAC) protein complex, one loaded with PHD fingers.

Along the way, Lindsey drew heavily upon the "awesome power of yeast genetics" in a lab that is not known for taking genetic approaches. And while the biological function of her complex proved stubbornly unwilling to reveal its secrets, patience and perseverance on her part suggested a novel role in connecting stress- and starvation-induced responses, exactly what most graduate students encounter at some point during their thesis work — her version of yeast's *Hunger Games*.

When she wasn't helping herself accomplish her science goals, she was helping others, raising the bar as being one of the most dependable Allis lab citizens, someone who was often our lab's go-to English expert.

Soon after joining the lab, Lindsey had me "in stitches" with another hobby — literally. As luck would have it, Lindsey drew my name in her first lab Secret Santa exchange, putting remarkable pressure on her to come up with something special. But, as with her science, Lindsey more than rose to the challenge, surprising me with an amazing cross-stitched nucleosome. Displayed proudly in my office, it reads, "Nucleosome Sweet Nucleosome." I can't imagine how many hours went into this amazing gift, but I immediately took myself out of the Secret Santa pool, setting my sights on trying to complete my own cross-stitch for her by the end of her thesis.

In truth, I never finished Lindsey's cross-stitch present, but I gave it to her anyway, with string and a needle attached. Knowing Lindsey, she will find the time to finish this project and to do more good science. At any point, she is welcome to share her hobbies by returning to Rockefeller and her Ph.D. lab, her old "Home Sweet Home."

Jacob Joseph Banik

presented by Sean F. Brady

B.S., University of Massachusetts, Amherst
M.Sc., University of East Anglia
Efforts Toward the Production of Novel Natural Products from Uncultured Soil Microbes

Jacob was part of our Tri-Institutional Chemical Biology Program, a unique program in which students spend their first year on the Cornell main campus in upstate New York. When I first met with Jacob to discuss joining the lab, he was worried about settling his young family in New York City instead of Ithaca for graduate school. He wasn't sure how a small town guy like himself would fit in with Upper East Side city slickers. In the end, he really had nothing to worry about as he and his family quickly adapted to the city, and he proceeded to excel in his graduate studies.

Jacob's graduate thesis work was one of the first studies to show that previously uncultured bacteria found in soil likely produce a tremendous diversity of still, as yet, undiscovered antibiotics. In fact, his work suggests that if you walked across the grass to get to graduation, you probably stepped on a multitude of bacteria that are capable of producing new versions of the some of the most important antibiotics used in the clinic today.

In addition to expanding the repertoire of known antibiotics during his graduate career, Jacob and his wife also expanded the size of their young family with the addition of two daughters. I'm not sure, but perhaps his role as our lab's rule enforcer, a role I think he truly relished, was honed from lessons he learned while raising his young daughters, or perhaps from the time he spent as a bouncer before he came to Rockefeller.

Upon finishing his Ph.D. work, Jacob returned home to Pennsylvania where he is now using his analytical chemistry skills to help safeguard the local environment. We wish Jacob and his family the best in all of their future endeavors.

Rudy Bellani

presented by Cori Bargmann on behalf of Fernando Nottebohm

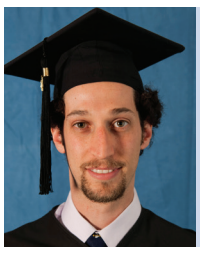
B.S., Arizona State University
Vocal Handedness: The Emergence of Lateralization at Fledging

Humans and songbirds share the ability to communicate through complex vocalizations that they learn from tutors in their own species. Rudy Bellani's Ph.D. thesis with Fernando Nottebohm and Tao Sun examined the earliest vocalizations of young canaries, who, like young humans, first babble and beg for food from their parents before they mature to singing their beautiful songs.

Rudy mapped the developmental trajectory from immature to more mature song patterns, showing a key transition as the birds make their first moves toward leaving the nest. He found that, like human speech, early canary vocalizations preferentially rely on the left brain compared to the right brain — a truly astonishing observation suggesting that complex brain systems have recognizable similarities in organization in animals as different as birds and humans.

Rudy Bellani came to Rockefeller from Bolivia by way of Arizona, and he is a force of science and a force of nature. In addition to his research, he has used his time at Rockefeller to provide mentorship to undergraduates and high school students from non-science backgrounds, and to write regularly in the student-run newspaper, *Natural Selections*. He knows that science and life are compatible: a key result in Rudy's thesis came about accidentally after a New York culinary excursion made him miss a feeding session with the canaries.

Rudy's enthusiasm for ideas, science and life have enriched us all during his years here.



Andrés Bendesky

presented by Cori Bargmann

Licenciatura de Médico Cirujano, Universidad Nacional Autónoma de México
Genetic Variation in Neurotransmitter Receptors Generates Behavioral Diversity

Leif Ericson, Ferdinand Magellan, Roald Amundsen. It is hard to imagine what prompted these men to leave the relative comforts of Europe in search of Vinland, a Western sea route to Asia, or the North and South Poles, respectively. But foraging theory tells us that the optimum behavior for a clever individual is to abandon a depleting resource before it is entirely gone, a strategy that enhances the chances of being the first to discover new and profitable resources.

As a graduate student, Andrés Bendesky devoted himself to understanding why some individuals take risks to explore new worlds, while others cautiously remain at home. Studying this decision in the nematode worm *Caenorhabditis elegans*, he found natural genetic variants that made different individuals footloose or sedentary. One affected a gene called *tyra-3*, which encodes a G protein coupled receptor related to the adrenergic receptors that regulate our own arousal levels. Andrés's studies of *tyra-3* provide a solution to a missing piece of the nature-nurture puzzle: this gene that regulates an innate tendency to abandon a depleting environment exerts its effects in the same neurons that evaluate the external quality of the environment — evidence that even for worms, individual decisions are all in how you look at things.

Andrés is an elegant, well read and artistically sophisticated intellectual who came to Rockefeller from Mexico City — a distance suggesting that he is a bit of an explorer himself. Andrés's intellectual explorations led to new and profitable discoveries that enrich our understanding of the genetics of behavior. Accompanied by his loyal dachshund Julio, and soon to be joined by his wife-to-be Sarah, Andrés is now exploring a new environment in the Hoekstra lab at Harvard, studying genetic variation in the social behavior of mice.

Elyse Blum

presented by Shai Shaham

A.B., Mount Holyoke College
Control of a Non-apoptotic Developmental Cell Death in Caenorhabditis elegans *by a Polyglutamine-repeat Protein*

Elyse is graduating today after making an important contribution to the scientific community: characterizing a novel molecular machinery that tells cells when their time is up, when they should throw in the towel and when they should die. The implications of her studies may be profound, and may allow us eventually to understand animal and human development and disease in a new light.

I first met Elyse when she interviewed with me for a research assistant position, fresh out of college. I was disappointed that she ended up in another lab. But I would only remain crestfallen for a few years … she eventually joined my lab, as a graduate student.

Here I became privy not only to her methodical scientific approach, but to her fearlessness in the culinary sciences. Her path in science has been meandering, as, it seems, are her adventures with food. And these have sometimes intersected. A group meeting involving genetic analysis, a juicer, beets and fennel comes to mind. Elyse continues her travels in science, in new directions, with new possibilities, and it will be exciting to see how these develop and what sumptuous delights may emerge.

Guillaume Charron

presented by Howard C. Hang

B.Sc., M.Sc., University of Montreal
Chemical Reporters for Investigating Lipidated Proteins at the Host–Pathogen Interface

Guillaume came to Rockefeller as a well-trained chemist from Montreal hoping to use his talents to study biology. As a new assistant professor hoping to use chemistry to explore how our immune system deals with microbial pathogens, we were well matched in our naiveté and adventurous spirit.

Because the membrane interface of our cells is often the first line of defense against microbes, Guillaume and I wondered if there were lipid-modified proteins in host membranes that could help protect us from harmful pathogens. Toward this goal, Guillaume's chemistry talents were just what we needed, as he was able to synthesize a series of designer lipids that allowed us to visualize and discover new lipid-modified proteins in immune cells.

To complete his thesis studies, Guillaume demonstrated that the membrane targeting of key proteins in our immune system is crucial for preventing viral infections. Guillaume's work has not only provided general tools for researchers interested in studying lipid-modified proteins, but has also revealed that the recruitment of specific antiviral factors to membranes is important for host defense — a feature that we may one day exploit for the design of new antiviral therapies.

I have been fortunate to have Guillaume join me in the early days of my lab. I wish him the best as he sets out for new and exciting endeavors.

Jeffrey William Craig*

presented by Sean F. Brady

B.A., M.A., Johns Hopkins University
The Application of Functional Metagenomics to Natural Products Research

From the first time that I met with Jeff, who is a student in our Tri-Institutional M.D.-Ph.D. program, all the way through his thesis defense four and a half years later, his enthusiasm for science and intellectual rigor have been truly refreshing. Even before officially joining the lab, he was arguably more familiar with the scientific literature in our field than just about anyone I had ever met. Fortunately for both myself and the other members of the group, Jeff's excitement for science extended far beyond his own work, as he seemed to cherish the role of mentoring others with their experiments, manuscript writing and presentation skills.

In the case of his own research, Jeff was so meticulous in the planning and execution of his experiments that something rare happened — most of what he tried at the bench actually worked; a fact that was not lost on his younger colleagues, as they gave him the nickname "lab hero."

Our lab is broadly interested in studying the large fraction of environmental bacteria that we now know cannot be easily cultured. Jeff's graduate thesis work showed that at the time, the best model systems used to functionally study DNA from this vast collection of unknown environmental bacteria were completely inadequate. He went on to develop a number of innovative solutions for improving the toolset that exists for studying these underexplored organisms and used his new tools to explore the small molecules and antibiotics produced by uncultured soil bacteria.

Jeff is now back in medical school at Cornell, just across the street, where I am sure he is doing at least as well if not better than he did here. Although Jeff has not been gone long, both his willingness to help others and his intellectual rigor are sorely missed. We wish Jeff and his wife the best in their future endeavors.

Disan Schold Davis

presented by Sidney Strickland on behalf of Tom W. Muir

B.A., Carleton College
Characterization of the Central Cavity of a Potassium Channel: Helix Dipoles, Conformational Plasticity and Inhibition

Disan Davis "flipped out" approximately halfway through her thesis research at Rockefeller. In the lead up to that memorable event, which I will explain presently, Disan received her undergraduate degree in chemistry from Carleton College, in Minnesota, before joining the Tri-Institutional Graduate Program in Chemical Biology in the fall of 2006.

For her thesis research, Disan worked on a collaborative project between my group and that of Rod MacKinnon's — indeed, Rod and I have essentially co-advised Disan during her time here. Disan's project was extremely challenging: namely, to apply protein chemistry methods, along with x-ray crystallography and electrophysiology, to study the inner workings of the model potassium ion channel KcsA.

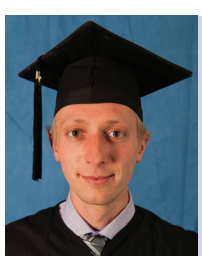
During the course of this work, Disan discovered, through detailed analysis of a series of high resolution crystal structures she had solved (dozens of structures in fact), that a key phenylalanine residue that lines the cavity of K^+ channels has a tendency to adopt an alternative rotameric conformation that results in the opening of a lateral porthole between the cavity and the surrounding lipid bilayer. Disan discovered that this "flipped Phe" conformation can be induced either by exposing the protein to certain lipids or through the binding of certain small molecules in the cavity of native channels.

These observations ultimately led to the novel idea that this "flipped Phe" conformation is important for the binding of certain drugs in the cavity of potassium channels, often with deleterious consequences for human health. Both Rod and I have been greatly impressed by the way Disan doggedly followed the various leads in this project, using whatever methods necessary, ultimately unearthing new insights into channel function.

Beyond the science, Disan has been an active, and at times overly ambitious, organizer of Muir lab recreational events — none more so than the infamous Muir lab synchronized swimming episode. Disan, it turns out, is an accomplished synchronized swimmer and as such thought that having the lab engage in this activity would be a good exercise in group bonding. Scotsmen are of course well-known for their grace of movement, nonetheless I am sure the sight of her supervisor engaged in un-synchronized drowning is something she will take with her to the grave.

Disan is a passionate and highly capable teacher and has been engaged in the various mentorship programs offered during her time at Rockefeller. For example, Disan was heavily involved in a national high school student science outreach program (the Catalyst Program) that I was associated with. This required that she act as a mentor to a series of talented high-school seniors who spent a year working in my laboratory in their spare time. Disan was fantastic at this, dedicated to and patient with the students, all of whom have now gone on to major in science at top-flight universities. Disan was an inspirational mentor to these kids and indeed, I am thrilled to say, she will join the science faculty of the Hunter College High School here in New York this fall.

We of course wish her every success in this endeavor and trust that she will obtain parental permission before taking the students swimming.



Simon Elsässer

presented by C. David Allis

Diplom, Eberhard Karls Universität Tübingen
Dissecting Mammalian Replication-independent Chromatin Assembly — Biochemical and Structural Studies on the H3.3-specific Histone Chaperones HIRA and Daxx

One measure of a top-notch graduate student is that they finish their thesis work as the lab's "expert," someone who knows their particular area of research better than most in the lab, and certainly, me. This is true in Simon's case. He knows histone variant biology, and the corresponding machinery that deposits specialized H3 family members in target genomic loci, as well as anyone. Following a dream to ultimately solve the structure of H3.3 in a complex with its relevant chaperone, Simon spearheaded the biochemical approaches that soon led him to an unexpected, direct H3.3-binding partner, Daxx.

Simon's work helped to unlock, in exquisite molecular detail, secrets into how specific histone variants are recognized and dealt with in medically relevant pathways of chromatin remodeling that lie outside of DNA replication.

Although gifted as an experimentalist early on, I grew to think of Simon more as an equal and much more as complete lab member. He wrote grants and fellowships that were funded, gave talks at meetings that I could not attend, hosted speakers and visitors when I was traveling, and often took a lead role in the lab just making good things happen. He stepped up to the plate to lend a hand more times than I can count, rarely with hesitation and never missing a step.

Simon's next scientific "dance" will take place at the MRC Laboratory of Molecular Biology in Cambridge, where he will study chemical biology and protein engineering. As a seasoned Rockefeller grad student, I don't expect him to make many missteps in his postdoc lab. But should he need help, he is *the* person who knows how to find a chaperone in the cold room that could accompany him to any part of the dance. Whatever dance he attends, I know that the music will be sweet.

I have been known to say "Every amino acid in histones matters." Thanks to Simon's work, we are beginning to know just how true this sentence might be and how histone chaperones are able to choose their partner with remarkable taste and discrimination. Simon gets my vote for any future *Dancing with the Stars* contests. He will be missed.

Markus Grammel

presented by Howard C. Hang

Diplom, Technische Universität München
Chemical Reporters for Bacterial Pathogenesis and Beyond

Markus is having quite a spectacular 2012. In addition to receiving his doctorate today, he got married this year, started a new job, purchased a home and will soon become a father. Wow!

When Markus joined the lab, he was charged with the lofty goal of developing a general strategy to identify protein factors from bacteria that help pathogens like *Salmonella* infect our cells. This was quite challenging because we wanted to identify low levels of bacterial proteins that are only expressed or secreted during infection of host cells. Markus was up to the challenge, though, and designed an elegant strategy to uniquely label bacteria with amino acids carrying special tags, which allowed us to specifically visualize and capture these bacterial proteins from infected cells.

In addition to this, Markus devised a new method to profile host proteins that are inactivated by these secreted bacterial proteins. Markus's thesis studies have provided our laboratory and others with powerful new methods to identify and characterize bacterial proteins that disarm our defense mechanisms. This is exciting because some of these bacterial proteins might be good targets for preventing infections in the future.

It has been a pleasure having Markus in my lab. Given Markus's ability to successfully manage many projects for his thesis, I am sure he will do an excellent job with all the new responsibilities he has acquired this year.

Heeun Jang

presented by Cori Bargmann

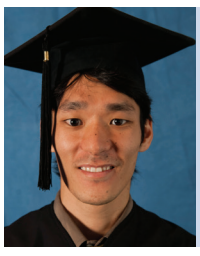
B.S., Pohang University of Science and Technology
The Neural Circuit for Behavioral Responses to Pheromone and Social Behavior in Caenorhabditis elegans

Heeun Jang came to Rockefeller from Korea with a passionate interest in the biology that underlies social behavior. In her thesis project, she asked a fundamental question that we have surely all asked ourselves: Why is it that sometimes I really want to be with other people, and sometimes I just can't stand the sight of anyone? This apparently trivial question goes to the heart of a fundamental aspect of social behavior — its sensitivity to context and internal emotional and motivational states.

Studying the nematode worm *Caenorhabditis elegans*, Heeun found that sociable worms find the odors of other worms (their pheromones) attractive, whereas solitary worms are appalled by the stench. To her surprise, these opposite behaviors are initiated by the same olfactory neurons, which sense worm odors and routes this information either toward approach behaviors or toward escape behaviors by differential use of alternative synaptic outputs.

The circuit for alternative behaviors is regulated by receptors for neuromodulatory peptides, and its ambivalent existence within the nervous system of all worms tells us that even the simplest animals have something like social free will.

In addition to her scientific creativity and intelligence, Heeun is a deeply humane person who will make the world a better place. She certainly made our lab a better place, in her gentle way. We join to congratulate Heeun, her husband Sung-Young Hong and her young son Lenny on the occasion of her graduation.



David J. Jordan

presented by Sidney Strickland on behalf of Stanislas Leibler

B.S.E., M.S., University of Pennsylvania
Analysis of Behavior in Populations of Swimming Microbes

Many organisms display behavior commonly called "roaming and dwelling." During dwelling periods, movement is slow and constrained to a small region of space, while roaming periods include faster excursions during which they explore larger regions. This behavior has been observed and studied in organisms as diverse as birds, worms and bacteria. Roaming and dwelling is often associated with some universal and basic life requirements, such as the search for food.

David Jordan arrived in New York from the University of Pennsylvania, where he studied engineering. At The Rockefeller University, David performed experiments on the roaming and dwelling of swimming microbes, in particular of the ciliates *Tetrahymena*. To do this, David developed an elegant new design of microfluidic chambers and a simple low cost video microscope based on Web cams.

With this system David gathered full-lifetime swimming trajectories from hundreds of single cells. He studied swimming behavior of individuals with different genetic backgrounds in various environmental conditions. By tracking individuals through several generations he was able to study the heritability of behavior in microbes. David also developed mathematical tools to analyze this large amount of data, which led to rather surprising results concerning behavioral variability, memory, plasticity and heritability. His work provides a first step toward an objective, large-scale statistical study of behavioral traits.

At the same time, David also performed his own "roaming and dwelling" outside of the lab. As an enthusiastic cook and a true gourmet, he explored the many restaurants and food markets of New York City. He dwelled in some of them for hours, leaving only in order to roam and explore other culinary enclaves. One of the things that makes David's thesis remarkable is the fact that he was able to keep these two passions well separated. His narratives about searching for food in New York City never compromised his rigorous study of microbial swimming behavior.

Barbara Juncosa

presented by Patricia Ryan on behalf of Vincent A. Fischetti

B.S., University of Miami
The Dynamic Streptococcus pyogenes *Transcriptome in the Host Cell Environment and Contributions by Phage*

At Rockefeller University, we expect our graduate students to be the brightest of the bright and the best of the best. Nothing, however, could have prepared me for Barbara Juncosa's level of talent. Barbara joined the lab of Vince Fischetti and was immediately liked by everyone — with her warm personality, it would have been hard *not* to like Barbara.

Behind the calm exterior was a passionate and driven scientist who tackled a dissertation project that most postdocs would not attempt. Barbara's studies on the initial interaction between group A streptococci and human throat tissue elucidated, on a molecular level, elegant sets of genetic switches and patterns of regulation that govern the ability of the bacterium to colonize the throat, leading to the onset of strep throat infections. This collection of data is the first of its kind; a seminal body of work that will, without doubt, have great relevance and continued reference in our field for years to come. Never before have we had such a detailed view of the dynamic interaction that occurs between these bacteria and the human host.

But Barbara's passions extend far beyond the lab bench and into the realm of science journalism and mass media. In her "spare" time, she was awarded a AAAS fellowship with *Scientific American*, where she interned as a science writer, and spent part of a summer in Banff, British Columbia, with Discovery Canada producing her own documentary. She spent another summer as an intern with *National Geographic*.

Her graduate studies, however, never took a back seat. On the contrary, her complex, 515-page dissertation is testament to her research accomplishments, as are the three competitive fellowships she was awarded to support her research. Her personal life also flourished at Rockefeller, as she married her high school sweetheart, Raul, in 2006. Together they will soon begin their new journey as they move to California, and Barbie begins her new role as an assistant professor of microbiology at Citrus College. She will be missed tremendously!

Isaac Andrew Klein*

presented by Michel C. Nussenzweig

B.S., Cornell University
The Extent and Nature of Chromosomal Rearrangements in B Lymphocytes

Isaac Klein is a native of Brooklyn, New York. Isaac made the trek to Rockefeller by way of Cornell in Ithaca and then NYU Medical School, where he worked as a technician for two years in David Roth's laboratory before joining the Tri-Institutional M.D.-Ph.D. program.

There were some fabulous things about having Isaac in the laboratory. For example, Isaac brews his own beer, he is famous for his 2nd-prize-winning kosher barbecue chicken and he is a rabid fan of the New York Jets and would bring green brownies to the lab when his team was playing.

But beyond competitive barbecue contests, Isaac is a brilliant young scientist. He is witty, eager to engage and to give you his take on an idea or experiment, he thinks fast, and as befitting his origins, he also talks fast.

For his thesis Isaac developed a new method to study chromosome translocations. Chromosome translocations are genetic events responsible for most forms of human B cell lymphomas. Before Isaac developed his method there was no way to study these events in normal cells because, fortunately, they are very rare events. Isaac's work uncovered some of the fundamental rules that govern the initiation of these events. Because his experiments uncovered important basic insights into the genesis of translocations, his work was published in both *Cell* and *Nature*. Isaac is now back in medical school and will go on to residency training before returning to the laboratory.

Manuel Leonetti

presented by Seth A. Darst on behalf of Roderick MacKinnon

B.S., M.S., École Normale Supérieure
Structural and Functional Studies of SLO K^+ Channels: Mechanisms of Gating by Intracellular Signaling

As part of his master's degree at the École Normale Supérieure in Paris, Manuel Leonetti visited Rockefeller University for five months, at which time he worked on the chemical synthesis of a potassium channel. He apparently enjoyed that work because he then decided, much to my delight, to return to Rockefeller for his doctoral studies.

As a doctoral student Manuel worked on the atomic structure and function of a class of eukaryotic potassium channels called SLO channels. There are three main types: calcium-activated, sodium-activated and proton-activated. SLO channels are also activated by membrane voltage. We seek to understand these channels because they play very important roles in cell biology.

For example, the calcium-activated variety is important in connecting levels of intracellular calcium to electrical excitation, a connection that is central to nerve and muscle cell function. In another example, the proton-activated variety is required for fertility in sperm cells. When Manuel entered my laboratory we had no knowledge of the structure of any part of an SLO channel. Now through Manuel's work, carried out together with postdoctoral scientist Peng Yuan and research technician Hsiung Yi Chun, we have visualized the opened and closed structures of the calcium activation machinery and a single conformation of the proton activation machinery. Thus, through his doctoral research Manuel has made a major contribution to our understanding of an important class of ion channels.

Manuel has been a wonderful student, colleague and friend. He is deep-thinking, sharp-witted and passionate. Lab meetings and lab barbecues just won't be the same without him. We will miss him dearly. But for me personally the scientific training period is just the beginning of a lifelong friendship. I have threatened Manuel and all my students and postdocs with the prospect that when I become old I am going to spend my time visiting them. Manuel grew up in Provence, so I do hope he spends some time there for my visit.

Manisha Lotlikar

presented by Sidney Strickland on behalf of John McKinney

B.S., California Institute of Technology
Mycobacterial Metabolism: Insights into the Host Environment

Manisha Lotlikar has an adventurous spirit. This proved lucky for me because soon after she joined my lab I had to inform her of my decision to relocate to EPF Lausanne in Switzerland. At that point she could have jumped ship, but instead she chose to jump "the pond" and continue her thesis in my lab, focused on genetic analysis of central metabolism

in *Mycobacterium tuberculosis*.

When Manisha began this project we assumed (naively, in retrospect) that attenuation caused by disruption of a metabolic pathway must be due to loss of the pathway per se. However, careful genetic analysis by Manisha pointed to a different interpretation. Specifically, Manisha hypothesized that attenuation might be caused by accumulation of toxic intermediates in a crippled biochemical pathway. It became clear that the only way to test this hypothesis was by making direct measurements of intracellular metabolite pools in mutant cells.

Once again, Manisha's adventurous spirit was equal to the challenge, as she had no qualms about "commuting" between Lausanne and Zürich in order to perform mass spectrometry-based metabolite profiling in the laboratory of Professor Uwe Sauer at ETH Zürich. It is fair to say that Manisha's research has uncovered surprising new insights into an area of biology that we thought we understood thoroughly, and has forced us to reevaluate the published scientific literature in this area. Not a bad legacy for a young scientist's first contribution!

Emily Rhodes Lowry

presented by Sidney Strickland

B.A., Barnard College

The GluK4 Kainate Receptor Subunit Regulates Mood, Memory and Excitotoxic Neurodegeneration

When Emily Lowry came to Rockefeller, she already had experience in neuroscience research. As a high school student, working at UCSF, and as an undergrad at Barnard, she made a deep impression on her mentors as a wonderfully gifted intellect and experimentalist. One mentor called her a "once in a decade science major."

For her thesis, Emily worked on a receptor that helps neurons receive chemical signals. The receptor is known as GluK4, and its exact role in the brain is not known. Mutations in this gene have been linked to schizophrenia, bipolar disorder and depression. Emily made mice that lacked GluK4 and studied them. In a remarkable series of experiments with extraordinary breadth — ranging from mouse genetics to molecular biology to animal behavior — she showed that these mice have reduced anxiety and despair, and impaired memory. Neurons in their brains are also protected from challenges that would normally kill the cells. Her results are seminal and provide novel insight into the possible origin of important neurological disorders.

Emily has, via nature and nurture, acquired a remarkable skill set as a scientist. She got some great DNA from her talented and supportive parents, and took advantage of opportunities to develop her intellect and expertise. So, she's very smart and hard-working, but she has other notable qualities. She's creative, skeptical of dogma and very importantly — and this quality I can personally attest to — she's not at all intimidated by authority figures.

Emily will be sorely missed in our lab by all, and especially me. We have a lab meeting lunch every week, and she and I have had terrific times during these meals. She's the epitome of modern, and by talking to her, I've felt like there was a chance for me to stay hip. Having publicly put myself and hip in the same sentence, I'm assuming she's making a face behind me right now!

Emily is off to Columbia University for a postdoc. We all expect great things from her in the future.

Laura Macro

presented by Sanford M. Simon

B.Sc., The University of Manchester

Conserved and Novel Properties of Clathrin-mediated Endocytosis in Dictyostelium discoideum

Life exists only
far from equilibrium
So true for the amoeba
dictyostelium:
To live they must feed
So they grab what they need
From what's floating a-
round in the medium

Iron enters all
cells with transferrin
Along with lipid,
integrin and dextrin
As membranes bend in
The cargo slips in
With the help of a
protein called clathrin

Clathrin's vital in
multi-celled metazoa
But not in single-
celled protozoa
Its role was a mystery
In evolutionary history
Must Laura archive
animals like Noah?
Why did it vary,
she tried to appraise
But clathrin's secrets
were hidden in haze
For then, like a dream,
Laura lit on a scheme
She'd study dicty,
Cause they go both ways

For these dicty lone
life is a truism
But they also show
heteromorphism
When hunger sets in
They merge with their kin
And become multi-
celled organisms

Their bodies become
one as they merge
Yet the fate of each
cell has to diverge
Its clathrin's needed
For growth that's unheeded
As new organelles
enlarge and emerge

While using this system,
Laura persisted
Remaining calm when
the dicty resisted
With ideas creative
And work authoritative.
She succeeded a-
'lone, unassisted

Besides her research
resplendent
On Laura our lab's
grown dependent
When someone's in need
She helps them succeed
Toward others she's
always attendant
From Montalcini and Curie
she's descendant
Her career in science?
Ascendant

From England she brought
tea across the sea
And worked hard to earn
a graduate degree
With accomplishments quite evident,
Mr. Carson, Mr. President,
I present Laura Macro, Ph.D.

Matthew M. Meredith

presented by Michel C. Nussenzweig

B.A., Colby College

The Expression of the Zinc Finger Transcription Factor zDC Defines the Classical Dendritic Cell Lineage

Matthew Meredith is a New Jersey native. Matthew grew up picking blueberries on his family's farm and brought his sunny optimism to Rockefeller from Middlebury College, where he was valedictorian.

It was wonderful to have Matthew in the laboratory. He is a talented experimentalist and insightful individual. For his thesis, Matthew picked the difficult problem of finding a molecular tool for distinguishing between dendritic cells and their closest relatives, the monocytes. Ralph Steinman discovered dendritic cells nearly 40 years ago. Part of the reason that it took so long to have this discovery recognized was that many scientists believed that dendritic cells were not significantly different from monocytes. In fact it was difficult to distinguish these cell types.

Matthew was able to find a transcription factor that is uniquely expressed on dendritic cells and make use of it to create genetically modified strains of mice that allowed him to delete dendritic cells but not monocytes. Matthew used this new tool to define the role of dendritic cells in immune responses. His work is summarized in two first-author papers featured on the cover of the *Journal of Experimental Medicine*. In the fall Matthew will be taking his considerable talents to Diane Mathis and Christophe Benoist's immunology laboratory at Harvard.

Marshall Curtis Miller*

presented by C. Erec Stebbins

B.A., Reed College

Structure Function Analysis of Adenosine Deaminase Acting on tRNA (ADAT2) from Trypanosoma brucei

It was the dreaded 3 a.m. call, and a groggy father answered the phone. "Hey Dad, guess where I am?" Given the hour, the father's first thought was, "Jail?"

Instead, he discovered that his son's conversational skills had impressed a tycoon and earned a trip for himself and several friends on a multimillion dollar yacht where he discussed politics and got hammered on expensive Scotch into the wee hours.

That young man's name was Marshall Miller, and he's been finding his way into amazing adventures his entire life.

One of those is the Tri-Institutional M.D.-Ph.D. program. Marshall came to my lab to perform the Ph.D. portion of this dual degree. His thesis focused on a class of enzymes of growing importance in what I like to think of as the "real-time" diversification of the genome. He also gave me the first opportunity in my 20-year career in science to collaborate with my wife, Nina, and her laboratory here at Rockefeller.

The information of life is dynamic. Nina's lab is studying the enzymes that modify the nucleic acids DNA and RNA to change informational content. One model organism excellent for this is the African trypanosome, which has evolved clever methods to alter its genomic structure to fool our immune system.

Marshall used a technique called x-ray crystallography to take molecular images of one such enzyme that modifies RNA to alter the translation of the genetic code. His work is opening doors towards an understanding of a critical class of molecules used by a wide range of organisms, including humans.

Marshall defended his dissertation on this project last December, and is now knee-deep in his M.D. internship program, which he hopes to finish in early 2013.

But of all Marshall's amazing adventures, he really struck gold with his beautiful family: his wife Ana and daughters Olivia and Camila. They have been one of the highlights of our annual lab barbecue, and I know fatherhood been a fun adventure for Marshall.

That is, until *he* gets that 3 a.m. call.

Miho Nakajima

presented by Nathaniel Heintz

B.S., M.S., The University of Tokyo

The Diversity of Cortical Interneurons

Miho Nakajima came to Rockefeller well-versed in molecular genetics, having already achieved a master's degree at the University of Tokyo. Miho chose for her doctoral studies to address what seems like a very simple question: What is a cell type? Although most of us would respond quickly that it is a group of cells with similar morphology and function, this definition clearly does not suffice. For example, a recent compendium on human cell types listed only about 200 different varieties, having grouped the last century of work on the hundreds of distinct electrically active cell classes under the single moniker "neuron."

Miho chose to address the cell type issue for an important class of cells in the cerebral cortex: inhibitory interneurons. These interesting cells make local connections within the cortex, and they have a vital role in modulating the output of the much more abundant, excitatory projection neurons. Abnormalities in subsets of cortical interneurons are thought to play key roles in disorders such as schizophrenia and depression. Although recent studies have suggested that there may be as many as 20 different types of cortical interneurons, it has been very difficult to get a precise genetic handle on any of these individual populations so that their molecular and functional properties can be explored in depth.

Miho set about this task with intelligence, energy, the most modern methodology that has thus far been developed for molecular characterization of cell types and advanced circuit mapping techniques that allow one to understand the specific position of a cell within neural circuitry. She generated dozens of bacTRAP transgenic mice, determined the molecular compositions of the cell types targeted in each of these lines, studied the anatomy and connectivity of these cells and generated new informatics strategies for parsing her data and comparing it to published studies.

The results of this Herculean task? Miho succeeded in refining further our knowledge of cortical interneuron types, both providing unique genetic handles for these cell populations and generating transgenic lines that will be useful for molecular phenotyping of these interesting cells in animal models of disease.

While these results amply demonstrate the unusual talents Miho possesses, it was her treatment of unexpected data that defined Miho in my eyes as an exceptional young scientist. She discovered that the receptor for oxytocin is tiled across the cerebral cortex to cre-

ate a uniform matrix for response to the hormone, even though the receptor is expressed in a heterogeneous population of interneurons. Amazing! If this turns out to be a general strategy for modulation of cortical function, Miho will have made a fundamental contribution to our understanding of the molecular biology of the nervous system.

In closing, I would like to thank Miho for all she has done for my laboratory. She is a truly generous young woman, and she is certain to continue to make important contributions to our knowledge of the brain.

Thomas S. Oh

presented by Charles M. Rice

B.S., Cornell University
Progress Towards Integrated Models of HCV Dynamics

Thomas (a.k.a. Tom) Oh was born in Philadelphia and raised in Philly suburbs, and attended Cornell University where he graduated with a degree in applied and engineering physics with a concentration in computer science. He then joined Princeton Optronics as an optical scientist and later as a product engineer before entering the Rockefeller University Ph.D. program.

As a Rockefeller student Tom was remarkably precocious, writing up a grant proposal as part of his virology course requirement, which he ended up submitting and getting funded. In the lab, he brought his keen intellect and quantitative skills to understanding how hepatitis C virus, a human pathogen affecting nearly 200 million people, regulates translation and amplification of its RNA genome versus packaging of this RNA into infectious virus particles. This work sets the stage for understanding how to combine new antiviral compounds to achieve higher cure rates for chronic hepatitis C.

Beyond his prowess at the bench and the computer Tom has many other interests (many of which I was unaware of). While his tinkering skills were evident, fixing broken computers and luminometers in the lab, Tom also served as the lab sound system engineer and DJ, codirected a short but hilarious film for a retiring lab manager and, with artistic flair, designed the current Rice lab T-shirt (presented to those departing who have survived the Rockefeller experience).

He is also a talented musician, playing piano, guitar, bass and drums. With all this going on, Tom still found time to keep his pet rabbit entertained and get married to his lovely wife, Ellen (and they are still married despite the fact that their honeymoon was postponed for a year while Tom finished his Ph.D. thesis). Suffice to say, this guy can do pretty much anything, and it has indeed been wonderful to have Tom in the lab.

Joseph Shannon Osmundson

presented by Seth A. Darst

B.A., Carleton College
M.S., Université Joseph Fourier Grenoble
Regulation of rRNA Promoters by Protein Factors

I distinctly remember my first encounter with Joe Osmundson — he was working in another lab at Rockefeller but needed to switch. He impressed me with a well thought out, interesting idea for a project that was tangentially related to our interests but was also very risky. I agreed to let Joe join the lab and work on his project, as long as he worked on another safety project. After several years of difficult but solid progress, we were forced to abandon Joe's project.

Fortunately, Joe also made progress on the other project that turned out to be full of surprises and was not such an easy ride after all. To complete this project, Joe developed and brought into the lab new technologies, and Joe is leaving with the most well-rounded scientific training.

Joe is well-rounded in other aspects of his life. He has an admirable interest in teaching, and he commits significant time and energy to organizing educational programs at local schools and mentoring undergrads, something that he does extremely well.

Joe will take up a one-year position at Vassar College, after which he will join the laboratory of Joe Thornton to reconstruct the characteristics of evolutionarily ancient proteins. He will be successful, although I hope he learns to clean up his lab bench. Joe also leaves the university holding a lab record that will be difficult to beat — the most nights spent in jail during his time at Rockefeller.

Kim J. Png

presented by Sidney Strickland on behalf of Sohail Tavazoie

B.S.E., Duke University
MicroRNAs in Breast Cancer Metastasis: Molecular Regulation of Endothelial Recruitment by Cancer Cells and Regulation of Metastasis Suppressor microRNAs

Kim is a very quick learner. It took her just three years to graduate with distinction from Duke as a biomedical engineer after having arrived as a foreign student from Singapore. It also took her very little time to gain comfort with cancer biology — a topic foreign to most biomedical engineers.

Being the first student of a new PI isn't the easiest of tasks either. Watching Kim school the boys on the basketball court my first year here provided me with a glimpse of her fearless spirit.

In my lab Kim studied the molecular and cellular mechanisms by which breast cancer cells spread — or metastasize — to distal organs. She focused on a small piece of RNA present in all of our cells that we had identified. She found that this small RNA prevents the metastatic spread of breast cancer by keeping the levels of three proteins low. When breast cancer cells lose this small RNA, these three proteins accumulate in cancer cells. When this happens, two of these proteins are released from cancer cells, sending a signal to endothelial cells that activates their movement toward the cancer cells. This recruitment of endothelial cells then triggers initiation of a new metastatic growth.

Kim also found that women whose breast cancers have low levels of this small RNA and consequently elevated levels of the three proteins it regulates have quite high rates of metastasis and death. This work, which Kim conducted in collaboration with her labmate Nils Halberg, has revealed a new role for endothelial cells in cancer progression that is independent of their established roles in providing blood flow to tumors. It has also identified new genes as targets of therapeutic inhibition in cancer.

Kim's attention to detail, her respect for negative or inexplicable data and her collaborative nature are just a few of the traits that will enable her continued success. She leaves Rockefeller to pursue postdoctoral work in Sydney Brenner's laboratory. Thank you for everything Kim, we will miss you.

Jessica Scott Rosenberg

presented by Hironori Funabiki on behalf of himself and Frederick R. Cross

B.A., New York University
Protein Phosphatase 1 at the Kinetochore Regulates Chromosome Segregation

Before you start your car, you must check that your passengers are all aboard and fasten their seatbelts. Starting the car before a passenger safely sits on a seat could be disastrous. Similarly, before a cell starts its cell division, there is a checking mechanism that delays the cell division before all the chromosomes are connected to their transporting machineries that distribute chromosomes equally to dividing cells. A failure in this event can be detrimental, since cell divisions prior to completion of chromosome segregation lead to an abnormal number of chromosomes, which commonly associates with cancers.

After graduating from NYU and joining Rockefeller, Jessica Rosenberg studied how this checking mechanism, the spindle assembly checkpoint, is silenced only when chromosomes are attached to their transporting machineries — combining the awesome powers of frog egg biochemistry and yeast genetics, under co-supervision of Professor Fred Cross and myself.

Jess revealed that recruitment of an enzyme called protein phosphatase 1 to the specific protein that is located at the boundary between chromosomes and the transporting machineries, microtubules, is absolutely essential to silence the spindle assembly checkpoint without disturbing the transporting machineries. In that car analogy, the enzyme acts as a part of the sensor at the seatbelt, without which the car won't start even though all the function for the car's motility is intact. Remarkably, this enzyme is known to be abundant in cells and plays multiple roles for a cell, such as metabolism, but Jess showed that recruitment of less than 0.1 percent of this enzyme to the microtubule-attachment site on a chromosome is critical, and a slight change in the amount at this site could cause lethal outcomes. Her study presents a nice framework for the future research in this enigmatic process of cell division.

Jess's creativity extended from her research to many other activities, such as her role as a lab pâtissier, baking a variety of cakes for lab events. One of the most memorable cakes that Jess created was the decoration cake, illustrating the nucleosome and the chromosomal passenger complex, on which our lab has been actively working. Jess's sense of humor, which is often expressed at her first slides of her presentations, has brought laughter to our lab. I'm sure that Jess will continue to act as a cheerleader for the scientific community.

Prerana Shrestha

presented by Nathaniel Heintz

B.S., Bates College
Molecular and Functional Characterization of Pyramidal Cell Types in Mouse Frontal Cortex

Wolfram Syndrome is a rare, multisystem disorder that is characterized by diabetes, optic atrophy, ataxia and severe disturbances of mood and affect. I am quite sure that as Prerana Shrestha made her way from Nepal to Bates College, where she graduated magna cum laude with a B.S. in biological chemistry, and as she entered the gates of Rockefeller, she had no idea that she would make an important contribution to our understanding of this devastating condition.

But in this age of discovery-based science, equipped with experimental strategies that allow us to peer into the very deep recesses of cells to understand their most closely kept secrets, talented young scientists like Prerana can sometimes reveal pathophysiological mechanisms in the course of their efforts to probe the fundamental complexities of biology. Basic science at its best, I would say!

Prerana chose for her dissertation the molecular characterization of cell types that compose the lamina of the cerebral cortex, eventually focusing on a thin layer of neurons present in the dense, outer supragranular layer. Using a combination of transgenic techniques and viral tracing methodologies, Prerana demonstrated that these interesting cells carry information both locally to deeper layer cortical neurons, and across the corpus callosum to the other side of the brain.

Although Prerana was among the very first to gain genetic access to specific laminar populations of cortical projection neurons, it was not until she succeeded in TRAP translational profiling of these cells that things really began to get interesting. Prerana discovered that this thin layer of cells, and no other cells in the cerebral cortex, express the causative gene for Wolfram Syndrome.

Using a combination of sophisticated genetic techniques and behavioral analysis, Prerana went on to demonstrate that Wfs1 is critical for the proper functioning of this interesting cell type, and that the mood swings and depression evident in Wolfram Syndrome patients most likely derive from the altered functions of this single cell type in the cerebral cortex. And based upon the molecular information she obtained, Prerana is now testing a very specific hypothesis that we believe can explain the cortical pathophysiology of this interesting syndrome. Quite a journey, I would say! I am fortunate to have been allowed to share it with this wonderful young scientist.

In closing, I will simply add that Prerana was cited this week in *The Huffington Post* as one of 30 high-profile neuroscientists whose "Twitter feeds are chockablock with interesting tweets." Wow! And I thought I was up to date!

Thibaud Taillefumier

presented by Marcelo O. Magnasco

B.S., École Polytechnique
M.S., Université Paris XI
Sample Path Analysis of Integrate-and-Fire Neurons

Thibaud Taillefumier attacked one of the most difficult problems in mathematical physics. As a quantity moves up and down, it eventually will cross any given level infinitely many times. Finding the very first time that it attains that level, which is called the first passage time problem, is a fiendishly difficult task that has been studied for 70 years by some of the most brilliant minds. This is because it models things as diverse as the onset of chemical reactions and the triggering of orders in the stock market. In neuroscience, one can see it in the fluctuating voltage of the membrane of a neuron, the triggering of an action potential — the fundamental mechanisms by which neurons communicate with one another.

During his thesis, Thibaud created extremely, extraordinarily elegant tools to study these problems that in my opinion have single-handedly advanced this field by about a decade. In

this work he was able to show that there is a transition in the mode in which neurons can fire action potentials to one another depending on how their input is structured.

However, as much as I would like to go on gushing about Thibaud's enormous intellect and ability, I have to tell you that his most defining quality is his totally intransigent approach to the truth. Thibaud simply faced no compromises in that sense.

He once thought he had found a potential flaw in a paper we had just had accepted at a major journal. Without even asking me, he called the journal and pulled the paper out of production. And for two months, he went over the paper, agonizing over every single detail of the proof, until I was finally able to convince him that there was no flaw.

At a time when many of our young scientists are constantly being tempted to choose flash over substance and sound bites over content, I find it totally refreshing and it gives me great hope that some of our young people are still pursuing the truth in this manner.

Lei Tan

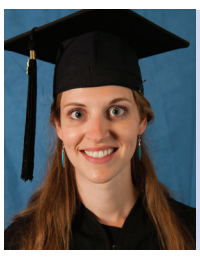
presented by Tarun Kapoor

B.S., Peking University
Examining Intracellular Phosphorylation Gradients during Cell Division

Life can be quite difficult for a cell. Its contents keep moving and its surroundings can be in constant flux. Yet the cell must somehow keep track of its center so that when it divides, it partitions its contents equally between two daughters. The cell has no obvious ruler to make quick measurements or a tag marking its center.

To examine how our cells can find their center during cell division, Lei Tan devised a clever microscopy approach. She developed sensors that allowed her to track chemical reactions at different locations and times in single living cells. Her studies reveal how an enzyme, called Aurora kinase, generates a spatial gradient of modified substrates that can act as a chemical map inside the cell. This map keeps track of the cell's middle, while all the contents rearrange and the surroundings fluctuate. Her work has shed new light on a fundamental cellular mechanism and has revealed the precise functions of an anti-cancer drug target.

Lei is a fearless researcher. She has also never been afraid to tell me what she, or what anyone else in my lab, thinks about me. We will all miss her very much.



Sarah Anne Wacker

presented by Tarun Kapoor

B.S., University of Richmond
Approaches to Study Small Molecule Inhibitors and Their Targets

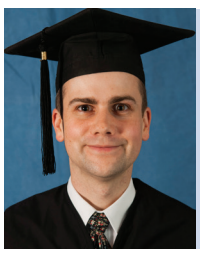
We need new and more effective drugs that can kill infectious agents or cancer cells. There have been many advances in the technologies we can use to find new drug candidates. Figuring out how these drugs work remains very difficult and most available approaches fail too often.

Sarah Wacker has developed a new approach, named DrugTargetSeq, which applies cutting-edge genome sequencing technology to analyze how a drug actually works. By analyzing entire genomes of human cells she identifies genetic alterations that appear at high frequency in drug-resistant cells. She then uses cell biology and biochemistry to find which of these genetic alterations lie in the drug's direct target. Using this approach she is able to achieve the "gold standard" in drug target validation.

Sarah did not stop here. She went on to develop a new mass spectrometry-based approach that identifies precisely where a drug binds its target.

Together, her studies address major challenges in modern drug discovery.

Sarah has consistently delivered more than she promised, both as a researcher and as a graduate student. We could also always count on her delivering better food than we could imagine for our lab events. We will all miss her very much.



Cameron Wellock

presented by George N. Reeke Jr.

B.Sc., Brock University
M.B.S., Keck Graduate Institute
Variability in Singing and in Song in the Zebra Finch

Cameron Wellock came to us from Brock University in Ontario, Canada, via the Tri-Institutional Training Program in Computational Biology and Medicine. When he came to me to discuss possibilities for thesis research, we talked about mutual interests in the fine muscle control that is involved in generating human speech and music performance. But after some thought, we could not see a practical way to study those questions in humans, so Cameron formulated a plan to work with songbirds instead.

He worked with zebra finches, recording some tens of thousands of hours of juvenile song at the Rockefeller University field research station in Millbrook, New York. These birds were not quite ready to perform at the Metropolitan Opera. Nonetheless, he developed software to listen to all those recordings and pick out the interesting parts. This software is now available on the internet for anyone to use. He measured the effect of listening to scrambled tutor song on the bird's learning and showed with a computer simulation that an area in the bird's forebrain that many thought acted just as a source of neuronal noise to create variability in song production might actually be the area where a key part of the learning takes place.

Cameron will be moving into another area of research, but his advances I am sure will provide much food for thought for those who follow him.

Sarah J. Whitcomb

presented by C. David Allis

B.A., Columbia University
Using "Designer" Nucleosomes to Study Enzymatic Crosstalk between Histone Ubiquitylation and Histone Methyltransferases

Those who mentor graduate students do so without a crystal ball; no one knows what projects will pan out and which will be "challenging." But all of these projects, the good ones and the less-good ones, are taken on by the students with passion and intelligence … this despite the long hours, false starts and setbacks. It surprises me at times that anyone will pursue this career, but the search for the answers is enough to motivate this special breed of people.

Sarah Whitcomb is one of those special people who has dedicated herself to the occupation of doing science, learning considerably from its frustrations and its rewards. It hasn't been an easy journey, in part because Sarah is a perfectionist. She thinks well and deeply about everything she does, and when things don't work, she isn't satisfied with just moving on.

Sarah's scientific passion evolved into the of study chromatin-mediated gene silencing, paying particular focus on relatively unexplored cross-talk relationships between two modifications of histone proteins: histone ubiquitinylation and downstream histone methylation. By synthesizing an elaborate set of chemically defined substrates, what we like to call "designer chromatin," Sarah methodically tested key reciprocal enzymes, showing the chromatin field which enzyme systems are stimulated by specific ubiquitinylation events and which are not.

Through it all, Sarah became comfortable with protein chemistry, not an easy feat for typical Allis lab members, owing this training to a wonderful collaboration with the Muir laboratory. Her future postdoctoral studies will study the effects of stress and other environmental effects in plants. Studying stress in plants as a postdoc is far better than being stressed as a grad student. Sarah's very nature means that she has many interests and passions, but we look forward to following her contributions to the "Green Revolution," drawing upon her talents and her Rockefeller education.

An influential Greek statesman, Pericles, once said, "Time is the wisest counselor of all." Sarah was plenty smart before grad school, but she is now time-tested by the challenges that face most graduate students. As her formal time at Rockefeller comes to an end, her acquired wisdom will serve her well, both inside and outside of science.

Peng Wu*

presented by Sidney Strickland on behalf of Titia de Lange

S.B., Massachusetts Institute of Technology
A Tail of Two Telomeres: Mechanisms That Ensure the Proper Terminal Structure of Mammalian Chromosome Ends

It is a generally known fact that human telomeres wither away with cell divisions due to the end-replication problem. Peng Wu, who came to our Tri-Institutional M.D.-Ph.D. program from MIT, not only showed that this doctrine is wrong but also discovered the actual reason why our telomeres shorten.

Peng came to our lab with an interest in the DNA component of telomeres, the elements that protect the ends of chromosomes from attack by DNA damage response pathways. She knew that at their very ends, telomeres were not made of double-stranded DNA like the rest of the chromosome, but featured a long, single-stranded protrusion — a tail — known to be important for telomere protection.

But how was this tail made? Peng attacked this question using a combination of mouse gene knockout approaches, cell biology and a remarkable technique that allowed her to separate telomeres copied by leading-strand DNA synthesis from those generated by lagging-strand DNA synthesis.

Over a three-year period of frantic experimentation, Peng produced a definitive study on how telomeres get their tails back after DNA replication. And it is this process of getting a new tail that is responsible for the shortening of our telomeres. Most of her work has not been published yet but I am pleased to report is about to be published in *Cell*.

Needless to say, Peng Wu is an intellectual and experimental force in the lab. For those of you who understand the nightmarish complexities of such experiments, she ran CsCl equilibrium density gradients on DNA derived from conditional triple knockout mouse embryo fibroblasts (which she derived herself) and did those experiments in triplicate. Others would have wilted just planning the experiments.

I suspect that Peng's ability to pull off this project has been helped by her hobbies. From her experience as a long distance runner, Peng may have developed her incredible stamina and ability to push herself. Peng is a lover of the arts, allowing her to appreciate the beauty in science and biology. And as an avid reader and a Scrabble maven, she writes so well that it was, at times, a little disheartening to be her thesis adviser because there was so little to correct.

Peng is now completing her medical training before she returns to the bench. Her friends and admirers in the de Lange lab and beyond are looking forward to her future achievements.

Mingzi Zhang

presented by Howard C. Hang

B.S., University of Wisconsin, Madison
Development and Application of Chemical Strategies to Study Protein Acylation in Eukaryotes

Mingzi is amongst an elite group of students that Singapore has sent abroad through the A*STAR program to learn science and engineering. They have chosen well with Mingzi.

It was clear when she joined my laboratory that she is a critical and deep thinker. Given our fascination with lipid-modified proteins, Mingzi was interested in the fundamental mechanisms that regulate how lipids are attached to proteins and how this influences the basic behavior of cells. For these studies, Mingzi turned to fission yeast — a powerful model system for studying eukaryotic cell biology.

With help from the Nurse laboratory here at Rockefeller, Mingzi made two important discoveries using fission yeast and our designer lipids. First, she demonstrated that regulated lipidation of a key signaling molecule helps fission yeast cells undergo sexual reproduction or meiosis. Second, Mingzi showed that a very precise level of the relevant lipidation enzyme was required to induce this dramatic cellular transition.

These observations are very exciting and provide an important framework for understanding how lipidation mechanisms control key signaling pathways in humans that are often perturbed during microbial infection, cancer and neurodegenerative diseases.

Beyond being an excellent scientist and terrific colleague, Mingzi is a world-class badminton player, which I got to witness first-hand when she crushed me 21 to 0. If all the A*STAR students are like Mingzi, then I think the future of science for Singapore is very bright.