

BenchMarks

THE COMMUNITY NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

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Convocation 2004!

Last week, for the 46th time in Rockefeller University history, faculty, students and staff dressed up and gathered in one room to celebrate the launch of the latest class of newly minted scientists.

The Doctor of Philosophy degree was awarded to 11 men and two women who have spent an average of 5.2 years at Rockefeller developing the skills they will need to succeed in the world of science. The graduates represent six countries in addition to the U.S.: Canada, China, Cyprus, Germany, Korea and Serbia.

Nine of the new Ph.D.s will go on to postdocs, two will return to medical school as part of the Tri-institutional M.D.-Ph.D. Program, and one will go into business. In addition, one graduate plans to travel to Africa or Asia to do field work before returning to medical school.

In the following pages, we reprint the speeches made by each of the graduates' mentors at the Convocation ceremony. (Two graduates, Paris A. Skourides of Ali Brivanlou's lab and Xiujie Wang of Terry Gaasterland's lab, received their degrees in absentia.)



More photos at www.rockefeller.edu/benchmarks



PHOTOS BY BRUCE GILBERT and ZACH VELLEUX

Honoring David Baltimore

Former Rockefeller president receives 2004 honorary doctorate

BY CATHY YARBROUGH

David Baltimore, who received his Ph.D. from Rockefeller in 1964, last week became the first Rockefeller University alumnus to receive the Honorary Doctor of Science degree, the university's most distinguished award.

"David Baltimore began his career at this institution and rose rapidly to become the most influential biologist of his generation," said President Paul Nurse at the June 8 Convocation ceremony. In fact, Baltimore completed his Ph.D. in "a blazing 18 months" and became a Nobel laureate at the age of 37.

In addition to sharing that honor, Nurse and Baltimore share a job description. Baltimore, who is currently president of the California Institute of Technology, was president of Rockefeller University from 1990 to 1991.

"David has brought this university great honor throughout his remarkable career, as researcher, educator, leader in science policy and master builder of scientific institutions," Nurse said.

Before speaking on "The Politics of Science," Baltimore told the Convocation audience that he applauded the freedom

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Paul Nurse, President
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Vincent Archambault

B.Sc., Université de Montréal

Proteomic and Functional Studies of the Cyclin-Cdk Module

Frederick R. Cross and Michael P. Rout (presented by Cross)

It's my pleasure to present to you, on behalf of myself and Mike Rout — we are co-advisors — Vincent Archambault, the first student to be presented to you today. Vincent is a great example of the kind of energy and abilities of a Rockefeller student. That's probably why he needed two advisors, to keep up with him.

After he came to Rockefeller, Vincent became interested in questions of how cell division is controlled. He chose to study the simple eukaryote carrier, baker's yeast, as a model system, combining proteomic and genetic approaches to identify and study novel binding partners in proteins that control the cell cycle.

This approach was somewhat unusual in that it required a number of different disciplines, and also, it required a major effort involving large-scale methodologies. These experiments are large scale, even on a simple physical measure, since they involve, among other things, hoisting about 40-liter flasks of yeast culture. And for the non-metrically minded, that's about 100 pounds plus.

But Vincent is a very fit individual and had no problem with this aspect of the work. A much more delicate aspect of the project, for which simple muscle strength would not suffice, involved mastering the mass spectrometry techniques of Brian Chait.

I should say that Brian could certainly have been considered a third advisor of Vincent, except I guess there wouldn't have been room on the program. We are all working hard to keep up with him. The mass spec methods required a lot of delicate work. I'm not really sure about that because Brian doesn't allow me, personal-

ly, to do any more than look at his instruments from across the room.

But Vincent mastered this whole technically and intellectually demanding set of procedures to identify some specific and very interesting protein-protein interactions. In the course of this work, Vincent concluded that he would need genetic methods, in addition to proteomics and biochemistry that he had already become excellent at, to characterize the significance of these protein-protein interactions.

And this transition in his project involved yet another step down in the size of muscle groups involved, because the main instruments here are the toothpick and the micro-dissecting needle. Also, careful thought about the logic of genetic epistasis and multiple mutant analysis are required. That involves some very small muscles inside the head that are sort of hard to get at but are very useful.

And then, these results fed back to the larger-scale biochemical questions that Vincent started with. It made a closed circle.

So in addition to the outstanding job Vincent did on his thesis research, he's also proved to be a great colleague to others in the laboratory. He is always happy to offer a helping hand and advice.

We will certainly be sorry to see him go, but we are happy to see him launched on what we are sure will be a very successful career in the future.

Mr. President, Mr. Fisher and honored guests — it is my pleasure to present to you Vincent Archambault.

Student speaker. Katie Hisert, who performed her Ph.D. research in both John McKinney's Rockefeller lab and Carl Nathan's Cornell lab, delivered the student Convocation address at a luncheon preceding the official Convocation ceremony. "Rockefeller scientists are acutely aware of the beauty in the world," Hisert said, calling her decision to study at Rockefeller a serendipitous one. "They are aware that beauty is just as likely to be found in the minutiae as it is in the broad picture. They believe the pathway is as fascinating as the destination."



Hwa Jin Baek

B.S., M.S., Seoul National University

Role of the Human TRAP/Mediator in Transcription

Robert G. Roeder

It's my pleasure to introduce Hwa Jin Baek. Hwa Jin was born and raised in Korea and received his undergraduate education at Seoul National University, where he developed his interest in molecular biology. After an additional two years as a research fellow at Samsung Research Institute, where he undertook a project that employed yeast genetic approaches, he joined The Rockefeller University's graduate program.

Not being overly sold on a term you often hear in this field — the awesome power of yeast genetics — he joined my lab in 1999 to work on a gene regulation problem in animal cells. His problem involved the further characterization of a giant multi-protein complex, composed of about 25 individual polypeptides that we had earlier shown to facilitate activation of specific genes, by DNA-binding regulatory proteins.

In essence, by acting as a bridge between the gene-specific factors and the enzymatic machinery that actually copies or transcribes the DNA, in rigorous and demanding biochemical approaches, Hwa Jin identified and characterized a new component of this complex.

More importantly, he discovered additional mechanisms by which

this so-called mediator complex stimulated transcription. This he did with remarkable skill and diligence, a great deal of independence, and on some occasions, a moderate amount of stubbornness.

This important work set the stage for an even deeper understanding of the very intricate gene control mechanisms of the cell, in this case, how a 25-subunit complex interfaces with another 50 or more proteins to turn on genes in a highly regulated manner.

On a more personal level, Hwa Jin has been a very congenial and helpful member of the laboratory. Potentially related, he met and married a fellow graduate student — Yun Kyoung Kang. And despite long hours in the laboratory between both of them, there arrived a beautiful daughter, Michelle, who is their pride and joy, and perhaps welcome relief from the exciting but demanding transcription work.

As you can see, Hwa Jin has been productive on several fronts and will be remembered in the lab both for his scientific ambitions and accomplishments and for his personal achievements.

President Nurse, Mr. Fisher and honored guests, I am pleased to present Hwa Jin Baek for the degree of Doctor of Philosophy.



David P. Bonnyay

B.A., Johns Hopkins University

Selective Targeting of Protein Antigens to DEC-205 on Dendritic Cells in the Steady State Leads to Tolerance in the CD8+ Compartment

Ralph M. Steinman

Ladies and gentlemen, David Bonnyay has studied a basic property of the immune system — tolerance. Tolerance has been as elusive in immunology as it has been in other spheres of life. Yet, in both instances, we know that tolerance can and must develop. So how does it happen?

How does the immune system charge into action to resist infection, but at the same time, remain silenced or tolerant of ourselves, our own proteins? David had a lead on how to silence the immune system to our harmless proteins, before infection strikes, so that the chance of an inappropriate auto-immune, or self-reaction, would not take place.

The lead he had involved a new approach from a student colleague, Daniel Hawiger, in Michel Nussenzweig's lab. David adopted this new approach. He directed the toleragen to a select group of cells, dendritic cells. But he did this in the steady state, which means in the absence of any other perturbant. By quietly and specifically delivering the protein to dendritic cells, David could silence the immune response. In effect, tolerance requires a gentle interaction with dendritic cells, without provoking them. This seems like a good

strategy for tolerance in general, don't you think?

David's signature feature is his wonderful disposition, frankly, the kind every parent wants his or her child to bring home. His personality really reflects his work: remarkable tolerance, with all of its components.

Since he helped us explain immune tolerance, I'd like to speculate a little bit about how his personal tolerance might have come about. It might have been due to the fact that he grew up in different parts of the world. He went to school in the U.K. and Holland, and even had to learn to speak Dutch. Furthermore, he met a mate, Jennifer, with a demeanor that's equally warm to his own. So maybe a breadth of exposure and a good partner are pathways to tolerance.

David is now pursuing a different track from most of our graduates. He is already in the business world, dealing with exciting new pharmaceuticals for cancer. We are impressed with the zest and assurance that he is showing for this new activity. And we are sure he will continue to make us proud.

President Nurse, Mr. Fisher, honored guests — it's a pleasure to present David Bonnyay the degree of Doctor of Philosophy.



Katherine B. Hisert

Sc.B., Brown University

Differential Screening in Immunodeficient Mice Reveals Bacterial Enzymes with Unexpected Roles in Host-Pathogen Interactions

John D. McKinney and Carl Nathan (presented by McKinney)

Among biomedical research institutions, Rockefeller University is regarded as something of a singleton. People use words commonly like "unique" and "unconventional" and even "eccentric" to describe our peculiar academic culture, and sometimes they apply these epithets to us personally.

There are a number of reasons for this, I think, including our small but very diverse faculty, our near total lack of departmental structure, and our commitment and our enthusiasm for interdisciplinary studies. But if I personally had to single out the one attribute that I believe really defines us as an institution, I would say that Rockefeller is a place that believes and invests in the power of the individual — the power to explore, to discover, to create and ultimately to change the world for the better. Rockefeller is an institution that supports innovative thinking and risk-taking, where individuals are actually encouraged to push the envelope rather than simply to stick to the safe and the sure path.

I think Katie Hisert's graduate career at Rockefeller provides an excellent illustration of that peculiar philosophy. Katie came to us from Brown University, where she had acquired a solid background in basic immunology. Her undergraduate research project had focused on murine immune responses to lymphocytic choriomeningitis virus, which is a superb model system for studying basic immune responses during infection, but it's hardly, of course, an important cause of global morbidity and mortality, unless you are a mouse, but no one is asking their opinion.

When she matriculated in our Tri-institutional M.D.-Ph.D. Program, Katie was very keen to apply the knowledge and skills she had acquired at Brown to a more medically relevant organism. But at the same time, she was reluctant to forego the tremendous advantages that model systems do have to offer.

Katie did a rotation in Carl Nathan's lab at Weill Medical College, focused on the model organism *Salmonella typhimurium*, which is probably the most-studied and best-understood of all bacterial pathogens. She also did a rotation in my lab here at Rockefeller, focused on the pathogenesis of *Mycobacterium tuberculosis* — the etiologic agent of TB, which is not so well understood as *Salmonella*. Of course, ultimately she had to make a choice to go with the model or the real deal.

And in the end, she came up with a really gutsy and creative solution to this dilemma, I think. Basically, she decided to have her cake and to eat it too. She realized that the fundamental questions that Carl's lab was asking in *Salmonella*, and that my lab was asking in *Mycobacterium*, were very closely related. And she opted to pursue a dual thesis, working simultaneously in both labs. Now this strategy, of

course, didn't make Katie's life any easier. Most students find it quite enough having to cope with just one project and one very demanding mentor, not to mention two.

But I'd like to think, and in fact, I would say I'm convinced, that Katie's training experience overall — thanks to this unusual dual track — was both broader and deeper than what either of our labs, mine or Carl's, could have provided to her.

Katie, it was not an easy path that you chose, but you have navigated it successfully to the end. And on the occasion of your graduation today, I salute you for your courage and creativity in defining your own path. I also salute Rockefeller University for allowing, and even encouraging Katie to embrace that risk.

Of course, the story doesn't end here. And true to form, as we heard already from Dean Strickland earlier today, Katie has already bucked the trend and mapped out a rather unique path for herself in medical school, to which she is returning now. She has obtained permission to devote part of her first-year studies in medical school to field studies on infectious diseases in impoverished communities in Southeast Asia and in Sub-Saharan Africa.

As a personal aside, Katie, I just want to say how very proud and enthused I am that you have taken this very unconventional choice and this very unusual path on your own, despite the considerable obstacles and risks that you face. In that spirit, I would like to present you with one last small token of my esteem, which I hope you will find as inspiring as I did.

It's this book, which is modestly entitled *How To Change The World*.

What it is, it's a history, actually, of Ashoka, which you may have heard of, which is a philanthropic NGO that was founded a number of years ago by Bill Drayton, the purpose of which was to identify and support so-called social entrepreneurs in all corners of the globe.

These are people you won't hear about on the evening news. But their ideas are already changing the human condition around the world, in 1,000 very meaningful ways. They are, and I quote from the sleeve of the book — "the driven, creative individuals who question the status quo, exploit new opportunities, refuse to give up, and remake the world for the better."

Katie, I believe that you have all the right stuff to join the ranks of these successful social entrepreneurs, which includes, of course, a newly minted Ph.D. from Rockefeller University, which ought to be an asset. And I look forward to following the trajectory of what I fully expect to be a brilliant career in biomedical sciences devoted to the benefit of humanity.

Mr. President, Mr. Fisher and honored guests, it is my pleasure and privilege to present to you Ms. Katie Hisert.



Gown and out. Rockefeller's purchasing department rented 114 caps and gowns and 74 hoods for students and other marchers to wear for the procession.



André Hoelz

Diplom, Universität Freiburg
Structure Function Relationship of the Serine/Threonine Protein Kinases PAK and CaMKII
 John Kuriyan (presented by Thomas P. Sakmar)

In preparing for this address, I did what I always do: I researched my topic. In this case, André Hoelz. I reviewed André's thesis, his published papers, his graduate school application and his transcripts from Freiburg University in Germany.

So far, so good.

But then I asked five or six people in my lab whom André had worked with over the past three years for advice. "Is there anything I should say about André next week at convocation?" I asked.

All I got in reply was four smiles and two grins.

People in my lab, when confronted with the prospect of describing André, were speechless. And so it falls to me to put into words the story of André Hoelz, Rockefeller University chapter.

As I think about it, André has three defining sets of qualities. He is dedicated and loyal. He is perseverant and stubborn. And scientifically, he is what I will call "kinase-centric."

In the kinase-centric view of the world, everything is under the gravitational influence of a particular class of enzymes, called kinases, that transfer chemical groups called phosphates, from ATP, the energy currency of cells, to proteins. André purified, crystallized and solved the x-ray structures of the association domain of CaM kinase II, and two forms of PAK (the p21-activated kinase). He started his work in John Kuriyan's laboratory — John was his official thesis research mentor — and finished up in my lab when John moved to Berkeley.

(It remains a mystery why no crystals of CaM kinase II ever grew on the third floor of the Rockefeller Research Laboratory

building in John's lab, but grew like gangbusters in my lab on the fifth floor.)

The structure of the CaM kinase II domain was particularly beautiful. Rather than the usual single lump of electron density, the CaM kinase II crystal shows a magnificent tetradecameric higher order structure — two sets of seven proteins stacked face-to-face to form a dual ring. The dual ring structure suggests a molecular rotor and clutch mechanism that has very important implications for understanding how calcium influx at the postsynaptic terminals in neurons in the brain regulates signal transduction. The beautiful structure, solved almost single-handedly by André, illustrates the cover of an issue of the journal *Molecular Cell*.

So, it is no wonder that Andre seems obsessed by memories of kinases past and future.

I really do not have the time to present a high-resolution analysis of André, the man. But André has a rare combination of childlike enthusiasm, intellectual rigor, work ethic and dedication, all qualities that are vital to creative science. And I can say, with complete candor, that he more than any person in the past 10 years has changed the direction of my research program — almost solely through force of will.

André is a force to be reckoned with. He is energy unlimited. And one of the things I like most about André is that he dedicated his dissertation to his girlfriend, Stephanie.

Mr. Fisher, President Nurse, ladies and gentleman, it is my privilege and honor to present to you André Hoelz.

Lining up. Faculty and staff — including Peter Mombaerts (*center*) — marched ahead of this year's graduates for the procession from Weiss to Caspary.



James A. Kappler

B.S., University of California, San Diego
A Genetic Screen in the Zebrafish for Mutations Affecting the Development and Function of the Acousticolateralis System
 A. James Hudspeth

Jim Kappler has a very distinguished genealogy. He is the offspring of two world-renowned immunologists. And this has left its imprint, obviously, in his character; he has superior intellect and wonderful technical skills.

But those of you who know immunology recognize that if you ask an immunologist even the time of day or how the weather is, you will get back a heap of Greek letters and symbols and acronyms. And this, being raised by two immunologists, puts Jim in the same category as children raised by wolves or other wild animals.

There's been a very definite effect on his pattern of speech, which ranges from reticent to mute. When I first encountered Jim, I was a bit worried about this, but it turns out that it makes him a delight to advise because, obviously, the responsibility of all the faculty is dealing with students' problems and helping them along. So when we would meet periodically, I would ask if everything was going okay.

And he would say — "Yes."

"Do you need anything? Is there anything I could do?"

"No."

And this has continued for four or five years, to my delight. He's done extremely well, for which I can take very little credit. Now, the one thing that does bring Jim alive, and even makes him slightly loquacious, is sports. He's heavily into athletics himself. He's the only person here on an athletic scholarship today.

He is a serious lacrosse player and also is interested in all kinds of other sports. And in fact, the things that really galvanize his activity are various athletic tournaments — the NCAA finals and the like — which make him appear hawking bets on various office pools for these sporting events.

And this attitude has also carried over to being really the main-spring of Jim's research career. We are interested in hearing: our lab

works on how hearing works normally, what goes wrong with it, and in the long run, what might be done to deal with that.

One of the approaches we've taken, with a great deal of help from Jim, is a genetic approach. We use zebrafish, which are mutagenized, and then examine the fish for those that have hearing problems as clues to what happens in problems in human hearing.

Now, genetics is in fact the application of sophisticated reasoning, statistical reasoning, really, to problems having to do with animal behavior. In essence, it's very much like horse racing or betting on any other kind of athletic event.

The great advantage of genetics over, say, betting on horses, is twofold. First, when genetics works, it's for the benefit of mankind and in fact, we can find useful things about hearing problems in humans from the sort of work that Jim and others in his group have done.

The other really nice thing about it is that, while both activities cost tens or hundreds of thousands of dollars, in genetics you use somebody else's money.

Specifically, Mr. Fisher's.

So Jim has really spearheaded, in our group, the development of all the statistical tools for the analysis of genetic alterations in zebrafish. He's been a wonderful asset to us all and has really helped, not only the other graduate students, but numerous postdocs in our group.

He's succeeded himself, already, in cloning one very interesting gene. And he is well on the way to locating, and probably has located, a second. So it's been a great pleasure having him with us, and we will look forward to his career in other areas of science.

So, Mr. President, Mr. Chairman, distinguished guests, it's a great privilege for me to present to you James Alexander Kappler, for the degree of Doctor of Philosophy.



Band and banners. Colored banners carried in the procession represented each of the labs from which students were graduating.

Kang Liu

B.S., Wuhan University

M.S., Fordham University

Dendritic Cell-mediated Presentation of Dying Cells In Vivo and its Immunological Consequences

Ralph M. Steinman

Ladies and gentlemen, I am an immunologist.

My student, Kang Liu, never stops talking. Actually, Kang retraced a characteristic path, I feel, in our graduate program. A lovely path that I quickly came to respect when I arrived here. At that time, there were three graduate students, who very much remind me of Kang, in the lab.

And I was struck by the fact that they were far from classical apprentices. Each was developing new methods — new areas of research within the lab — rather than pre-existing ones. If these students were apprentices, then they were learning the trade of discovery.

All three went on quickly to professorships in major institutions after leaving here. So Kang Liu walked into the lab and declared that she wanted to better understand how the immune system deals with tumors.

“Kang,” I said, “tumors are demanding enough, but they are different from our usual lab interest, which is infectious disease.” So Kang just went out on her own. She took apart the tumor problem, literally, by asking: what transpires if a tumor cell dies and is captured by dendritic cells?

Dendritic cells are sentinels. And normally, they have to alert the body that an infection is taking place. But Kang figured out how to study the sentinels during their capture of a dying tumor,

and in an intact animal.

Together with colleagues from Kyoto, she demonstrated the remarkable efficiency with which dendritic cells deliver proteins from tumor cells to the immune system. And then following this delivery, she documented two very different outcomes. On the one hand, she showed that the immune system could be silenced to the tumor.

And on the other hand, she was able to induce strong resistance to tumors by properly activating the dendritic cells. The latter findings on tumor resistance, I feel, are worthy of pursuit in patients.

So Kang Liu really made things happen. And I can’t overlook what happened on a trip home to China, early in her graduate school career. She sat next to a young faculty member from Hunter College — not a tourist, but an expert in Chinese history.

Well, the skies were very friendly. Love bloomed. Marriage to Richard ensued in Central Park, and a charming son has joined the lab family. Kang Liu begins her postdoctoral work on another area of immunology with Michel Nussenzweig, I suspect, shortly after this ceremony. We confidently await the future fruits of her ingenuity.

President Nurse, Mr. Fisher, honored guests — it’s a great delight to present Kang Liu for the degree of Doctor of Philosophy.



Hugs... André Hoelz celebrates with family following the ceremony.

Nebojsa B. Mirkovic

B.Sc., University of Belgrade

Structural Approach to Functional Characterization of Proteins and Amino Acid Replacements

Andrej Sali (presented by Brian T. Chait)



Andrej Sali, who was supervisor to Nebojsa Mirkovic, sends the following message:

I would like to begin by expressing regret for not being with you today. Nebojsa joined my laboratory at Rockefeller in 1999, and despite his background in biochemistry, decided that his thesis should be in computational biology. Over the past four years, he carried out a number of different projects. Let me mention just two of them here.

Nebojsa came up with the idea for his first project on his own. Just after the fly genome was published by Celera, he was thinking about doing a rotation with Arnold Levine, a co-discoverer of human p53, a protein central in the development of many cancers. So he asked the question whether the fly contains any p53-like proteins. He obtained a positive prediction, by a very difficult comparative modeling of a putative fly p53 based on the human structure and by observing the conservation of some key DNA binding residues. Subsequent biochemical and *in vivo* experiments confirmed the existence of the p53-like network in the fly. Nebojsa deserves the lion's share of the credit for this important discovery, which provides a useful genetic system for the further study of this critical network.

His main thesis project was aimed at developing a computational approach to predict functional effects of point mutations in proteins. Based on common knowledge about protein folding, stability and evolution, he formed a novel set of protein features that were

employed to explain or predict the impact of amino acid replacements on protein function. As Nebojsa remains a biologist at heart, he strived to apply his computational approach to interesting proteins, and found a great opportunity involving the human BRCA1 protein, mutations of which are a major cause of breast and ovarian cancers. Unfortunately, the cancer association of most of these mutations is unknown, which creates significant problems for genetic counseling. Working with Professor Alvaro Monteiro at Cornell Medical School, who produced and characterized a large number of mutations in BRCA1, Nebojsa successfully demonstrated the utility of his computational methods for annotating functional consequences of point mutations.

Andrej writes: I would like to conclude with an anecdote that illustrates one particularly intelligently quirky aspect of Nebojsa's character. Early on, Nebojsa had to learn some programming to process his data. He had a choice between the relatively simple Perl or the difficult Lisp. He chose Lisp, in all its complexity, because the manual was only 40 pages long, as opposed to the 200 pages of the Perl book. And, of course, he succeeded!

Nebojsa is currently a postdoc with Diana Murray at Cornell Medical School. Andrej writes: I thank him for his contributions to our research and wish him all the best for the future!

President Nurse, Mr. Fisher, honored guests — it is my pleasure to present to you Nebojsa Mirkovic for the degree of Doctor of Philosophy.

...and kisses. Katie Hisert and her mother.



Joshua Silverman

A.B., Princeton University

The ATM-dependent DNA Damage Response Function of Human Rf1
Titia de Lange (presented by Sidney Strickland)



Titia de Lange, who is unable to be here today, asked me to read the following:

Josh Silverman, born and raised in Florida, joined us as an M.D.-Ph.D. student after training in chemistry at Princeton. Josh is quite typical of the outstanding students in our Tri-institutional Program. His intelligence, willingness to think deeply, and ability to work hard are in keeping with the norm in this group of superlative students.

What distinguishes Josh from his peers is his ability to weather considerable set-backs.

Just after he joined my lab, there was an event that made me realize that Josh was able to perform under quite difficult conditions. It was November 1999, and Josh ran the New York City marathon. Although a little slower than usual, Josh finished the race and was in the lab the next day. But he complained of some abdominal pain and had himself checked out. Soon after that he underwent surgery. Turns out that he had been running the marathon with a hernia.

Josh's ability to reach the finish line under difficult circumstances served him well in the remarkably circuitous path of his progress

toward a Ph.D. We all know that odd things can happen at the bench even when experiments are carefully planned, but Josh's bad luck in experimental biology was so extensive that I was worried that it would dishearten him to the point of no return.

But Josh persisted through this period of rope-a-dope at the bench and succeeded in the end. Through a series of unanticipated discoveries, Josh identified a new DNA damage response factor that appears to have clinical relevance. Starting with what Josh thought would be the mammalian ortholog of a yeast telomeric protein, he ended up working out an entirely new branch of the ATM dependent DNA damage response.

Josh is now pursuing further training in medicine and will then go on to do postdoctoral research. Wherever he ends up, Josh will surely be appreciated not only for his keen scientific talents but also for his sense of humor, the warmth and support he brings to his family and friends, and his impeccable integrity both as a scientist and a member of any community.

Mr. President, Mr. Fisher and honored guests, it is my pleasure to present to you Joshua Silverman.



Family photo. Hwa Jin Baek, from Robert Roeder's lab, poses for photos with his daughter, Michelle.

Raymond Soccio

A.B., Harvard College

A Novel Subfamily of Three StAR-related Lipid Transfer Proteins that are Differentially-regulated and Function in Intracellular Cholesterol Metabolism

Jan L. Breslow

In my laboratory we try to figure out why some people get heart attacks at an early age while others never succumb. The causes of heart attacks are complex, with many genes involved, significant environmental factors and important gene-environment interactions. Currently, most research is aimed at understanding genetic or environmental effects on heart attack susceptibility. Very little effort or progress has been made in understanding gene-environment interactions, and Ray Soccio chose to address this problem for his thesis work.

Ray's approach was to feed mice diets low and high in cholesterol and, using microarrays, identify liver genes regulated by dietary cholesterol. In the course of his work, Ray identified a novel gene downregulated by dietary cholesterol, and the study of this gene and its related gene family comprised Ray's thesis. The gene Ray discovered codes for a protein that consists almost entirely of a START domain. This domain is 200 amino acids in length and can fold to form a hydrophobic pocket large enough to accommodate one molecule of cholesterol or phospholipid. Three genes with this motif had been described previously and Ray's discovery was the fourth, now called StarD4.

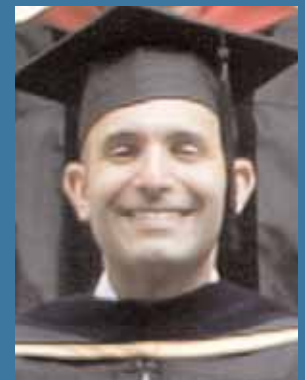
Ray worked out the x-ray crystal structure of StarD4, in collaboration with the Burley Laboratory, and he was also able to uncover two other close gene family members by database searching, named StarD5 and StarD6. Ray's studies strongly suggested that StarD4, D5 and D6 bind cholesterol and play important roles in intracellular cholesterol transport. Despite structural similarities, his studies of regulation of these genes suggested different functions. He found StarD4 and StarD5 expressed in many tissues, but StarD4, as previously mentioned, was downregulated by cholesterol, whereas StarD5

was upregulated by ER stress as part of the unfolded protein response. StarD6 is expressed only in mature sperm and StarD6 protein is localized to the mid-piece of the sperm tail, where it may play a role in sperm motility and male fertility.

In addition to his experimental work, Ray, with minimal help from me, published two important reviews. In the first, Ray used the completed human and mouse genomes to show there are 15 START domain containing genes in mammals, which are divisible into six subfamilies. He also identified START gene ancestors in the sequenced genomes of more primitive organisms. In his second review, just published, Ray summarized the literature concerning intracellular cholesterol metabolism. This important field is complex and often confusing and Ray's review should be quite helpful in this field of study.

On a personal level, I have thoroughly enjoyed working with Ray. He is a brilliant young man with unlimited potential for a career in biomedical science. He is a generous person and an excellent colleague. He makes everyone around him better and has had a tremendous positive impact on my whole laboratory. Ray entered the Tri-institutional M.D.-Ph.D. Program with his wife Leslie, who received her Ph.D. degree last week from Cornell. In his spare time Ray is a great runner and sports fan. As a New Englander, he roots passionately for the Boston Red Sox and has suffered a great deal from the "Curse of the Bambino." Even though I am an ardent Yankee fan, for Ray's sake I sometimes find myself rooting for his Red Sox, but please don't tell anyone.

Mr. President, Mr. Fisher and honored guests, it is my great pleasure to present to you Raymond Soccio for the degree of Doctor of Philosophy.



Frank Vollmer

Vordiplom, Universität Bayreuth

Diploma, University/Medical School Hannover

Single-molecule DNA Biochemistry, Genetic Circuits and Chromatin
Albert Joseph Libchaber

Frank Vollmer is an undergraduate who studied in Germany, Bayreuth University. When he came to my lab, a young biologist lost among physicists, he had some difficulties from which he recovered. He also recovered from his passion for motorbikes, which led to some bones broken.

Frank was interested in new techniques. He learned optics from Steve Arnold at Brooklyn Polytechnic Institute and built an optical set up to study the optical resonance of a glass sphere. The glass sphere is much larger than the wavelengths of light. It is a remarkable resonator for a mode trapped inside by total internal reflection and no losses, of course, in the glass.

Absorbed proteins or virus or bacteria, absorb on the surface

within the optical evanescent field of the light, shift the resonance frequency. This leads to an optical detection of any biological object. The ultimate sensitivity of this detector is that of one protein.

The response is linear in concentration for what are called Rayleigh particles — particles smaller than the wavelengths of light. The response is quadratic for Mie particles — particles larger than the wavelength of light.

This unique detector is Frank's own work. He will pursue his research as a fellow with the Roland Institute at Harvard University.

Mr. President, Mr. Fisher, I am glad to present Frank Vollmer for the degree of Doctor of Philosophy.



Mary Abraham awarded David Rockefeller Fellowship

Co-founder of *Natural Selections* recognized for promise as a scientist and a leader

BY BETSY HANSON

Mary Abraham, who discovered a new way for cells to die, is this year's recipient of the David Rockefeller Fellowship. The award was presented at a luncheon just before Convocation by the recipient of this year's honorary degree, Rockefeller University alumnus and past president David Baltimore.

Abraham, 25, joined Shai Shaham's Laboratory of Developmental Genetics two years ago and focuses her research on programmed cell death in the worm *C. elegans*.

Every organism creates new cells as it grows, but just as important to its survival — to the formation of organs, for example — is the death of certain cells at specific times during development. When it's time for a cell to self-destruct, genes that code for killer enzymes called caspases turn on, signaling the cell to die.

Abraham studies a cell called the linker cell that plays a role during male development in *C. elegans*: it guides the male gonad from the middle of the organism, where it forms, to the posterior. When this job is done, the linker cell dies — but caspase enzymes are not required; another not yet identified gene is needed for death to occur. "Linker cell death appears to be an unsolved case of cellular murder," says Abraham, who is searching for the genes responsible for this novel form of cell death.

"Mary is rigorous, attentive to detail and very imaginative — perhaps that's the most important thing that a scientist can be," says Shaham. "She's a smart and thoughtful person."

Abraham, who grew up in Northern Ireland, came to Rockefeller in 2001 after completing her B.A. and M.S. degrees in biochemistry at the University of Cambridge. While at Cambridge, she spent two summers doing research on *C. elegans* in laboratories at Johns Hopkins and Yale universities, experiences that made her consider coming to the United States for graduate school. Rockefeller appealed to her because of the flexibility of the graduate program.

"Another thing I liked was being at a university where there are lots of branches of science being pursued without a departmental structure," she says. "If you go to a graduate program in a microbiology department, for example, you don't get exposed to a Friday lecture on neuroscience."



Abraham, linkers. The David Rockefeller Fellowship recipient, who studies the "linker cell" that plays a role in male roundworm development, in the lab.

The cultural life of New York City was an additional attraction. "Above all, I adore going to the theater and in New York you are certainly spoiled for choice," she says. "Other favorites are the museums and art exhibitions."

Abraham is also an active contributor to Rockefeller's cultural life. With fellow graduate student Ian Berke and others, she launched the community newsletter *Natural Selections*, which began publishing in December 2003.

"Our motivation was to have a publication that would be open to written submissions from anyone on campus and would provide an outlet for writing that didn't exist. We felt that having articles written by community members would be a good way for people to get to know each other," says Abraham. "We also wanted to run types of articles that weren't available in the official newsletter — for

example, graduate student course reviews, people writing about their home countries, satire and so on."

In the coming years, Abraham hopes to grow and develop as a scientist. "I hope that I will be successful in uncovering the molecules and mechanisms responsible for the cell death that I am studying," she says. "Shai is a wonderful mentor — very clever, very encouraging, and he is someone who really loves science and that is very inspiring. The other people in the lab are also great to work with. And I think cell death is a really exciting biological problem."

The David Rockefeller Fellowship has been awarded annually since 1998 to an outstanding third-year student who demonstrates exceptional promise as a scientist and as a leader. The award, which was established by the university's alumni, consists of a one-year stipend and a monetary prize.

Baltimore *continued*

that Rockefeller provides "for a young person to follow his or her own nose."

"Science is an individual enterprise. It's an enterprise that's very much about people finding their passions, and Rockefeller is one of the rare places where you can do that," Baltimore said.

Baltimore's passion was in molecular biology. After graduating from Rockefeller, Baltimore generated research findings that "overturned a central assumption about how nature operates," explained Nurse. At the age of 37, Baltimore shared the 1975 Nobel Prize in medicine for revealing that

certain RNA viruses contain a previously unknown enzyme that enables these retroviruses to transcribe genetic information from RNA into DNA.

In the 1970s, the research of Baltimore and a few other leaders in molecular biology launched the biotechnical revolution. In

response to the scientific community's — and public's — concerns about the safety of biotechnology, Baltimore helped to organize the now famous Asilomar Conference that in 1975 recommended the first ethical and safety standards for the use of recombinant DNA technology.

In addition to being an active citizen of science, Baltimore has proven to be a superb administrator. He was instrumental in establishing the Whitehead Institute at MIT in 1982 and served as its first director. "Just as he had expanded his own laboratory to integrate studies in virology, immunology and molecular biology, David designed the Whitehead Institute as a new kind of research environment that would build bridges across disciplinary boundaries," said Nurse.

Subsequently, as president of Rockefeller University, Baltimore drew on his experiences as a student, as a young researcher and as an institutional leader. "He introduced many ideas here that took hold and prospered," said Nurse. "In particular, his emphasis on nurturing the careers of junior faculty members helped to build the vital Rockefeller University of today."

Baltimore's Convocation speech discussed three ways in which politics and science are tightly interwoven: the position of science in federal government's deliberations and policies; the need for trained personnel to maintain America's strength as a scientific powerhouse; and structuring science around more focused questions in order to apply advances in basic knowledge to deal with disease.



A return to Rockefeller. Alumnus and former president David Baltimore, recipient of this year's honorary degree, speaks at Convocation.