Sun Reflects on 20th Annual Retreat

by Bryan K-H. Sun

There’s an energetic buzz in the car—some mixture of Friday afternoon relief, the excitement of getting out of town, and the anticipation of the weekend retreat.

I’m driving up I-93 with Shannon McDonald (Year 3-Math), John Ng (Year 5-Biophysics), Rebecca Spencer (Year 6-BBS), and Tammy Chang (Year 9-Immunology). Wading through rush-hour traffic, we exchange tales of lab and the wards, update each other on who’s-going-into-what-residency and who-matched-where and who-joined-which-lab, ask each other about research progress, and argue whether Eminem is a genius or a fake. A back-of-the-napkin calculation tells us that we might just make it in time for dinner. The tollbooth looms, and exact change appears from collective pockets.

Twenty years ago, in a cool October just like this, the first M.D.-Ph.D. retreat was held at the Cape Cod Sea Camps, where students and faculty shared chilly cabins on the beach and cafeteria food about one mile’s walk inland. Since then, the retreat location has migrated to several other locations including the MBL at Woods Hole, and on one occasion, Linda Burnley’s house. Waterville Valley has been the retreat destination for the last five years. While having less rugged charm than the original retreat, it still aims to bring together faculty and students to share ideas about science, medicine, and careers.

We’ve made it. Well fed from dinner (with minutes to spare!) we head into the first set of talks that evening. As usual, there’s a wide breadth of research areas and
Every Dog, from page 1

frightening pace.

Dr. Chodosh earned his Ph.D. in the laboratory of Dr. Phillip Sharp at MIT, where he was among the first to perform DNA gel shift assays in mammalian cells, allowing him to identify some of the earliest promoter-specific mammalian transcription factors. His work, published in three separate Cell papers and a Science paper, was instrumental in establishing the eventually sprawling field of transcription factor biology. When he began identifying these DNA binding proteins, he remembers Dr. Sharp (whose picture hangs in Dr. Chodosh’s office) speculating, “There may be many more of these promoter-specific transcription factors than we thought. There may be as many as … TEN of these things.” Of course, hundreds are now known.

“I became interested in what I would call experiments of nature and, more specifically, how nature prevents breast cancer.”

After a residency in medicine and a fellowship in endocrinology at MGH, Dr. Chodosh joined Dr. Philip Leder’s lab at Harvard Medical School. “In the Leder lab,” explained Dr. Chodosh, “I became interested in what I would call experiments of nature and, more specifically, how nature prevents breast cancer.” Through Dr. Leder’s urging, Dr. Chodosh focused on the observation that women who have a child early in life have a significantly lower lifetime risk of developing breast cancer. This reduced risk likely stems from protective physiologic events that occur during full maturation of the mammary gland during pregnancy and lactation.

Cancer susceptibility, explains Dr. Chodosh, depends on the developmental stage of the gland at the time of the oncogenic insult. To study this relationship, the Chodosh lab designed a doxycycline-inducible transgenic mouse system, which has allowed them to activate oncogenes in mammary glands at various developmental time points, during which they could then examine cancer susceptibility. These studies are made possible by tight temporal control within their system, which provides over 100,000-fold induction of transgenes upon administration of doxycycline, resulting in clear glandular changes in 24 hours.

Working with mouse models inducibly overexpressing the MYC and Neu oncogenes, the Chodosh lab has made important findings, published in Nature Medicine and Cancer Cell, about late genetic events contributing to breast cancer progression. Though not having set out to study advanced stages of carcinogenesis, they found that after de-induction of either MYC or Neu, complete regression of most oncogene-induced tumors occurred. In the case of Neu-initiated primary mammary tumors, lung metastases were also reversible. Such tumor reversibility, initially shown in melanomas by Dr. Ronald DePinho, is exciting because it lends credence to the idea of treating cancer with pathway-specific drugs after tumors have already developed.

Even more exciting was Dr. Chodosh’s finding that of those tumors failing to regress after MYC de-induction, most had spontaneously acquired activating point mutations in the oncogene Kras2, yet not in its closely related family member Hras1. “This provides strong evidence,” says Dr. Chodosh “that tumors escape dependence on an initiating oncogene by preferred secondary pathways.” Their finding has important clinical implications because single drugs are almost never sufficient for curing cancer. If tumors become resistant to drugs by preferred secondary mutations that are known, one can potentially prevent tumor recurrence by simultaneously targeting these secondary pathways during initial treatment.

More recently, Dr. Chodosh has begun using DNA microarrays to study mechanisms of mammary oncogenesis. Such genomic studies have plunged his lab into the field of computational biology, which Dr. Chodosh says “keeps him young … or at least off street corners.” Using microarrays, the Chodosh lab has identified genes whose expression in the breast is permanently altered after an early first full-term pregnancy. Experiments are currently underway to study these genes as potential mediators for parity-induced protection against breast cancer.

Dr. Chodosh has continued seeing patients while maintaining an active research lab and hopes to see his career involve even more clinical work in the future. For example, he would love to study how parity affects endocrine function in humans and ultimately to perform clinical trials on hormonal chemoprevention regimens aimed at mimicking the protective effects of parity on breast cancer risk. Making the decision to pursue a career in both science and medicine, however, means that you “have to give some stuff up,” says Dr. Chodosh. “People will always be comparing you to others who do either science or medicine full time,” he explains. “You make some sacrifices for doing what you love.”

When I asked Dr. Chodosh about whether he had any advice to offer M.D.-Ph.D. students, who were not so far along in their careers yet still rapidly aging, he replied, “Follow your heart, and don’t worry about the time.”
Journal Club Studies the Classics

by John W. Hanna and Mauro D. Zappaterra

This past summer, the first and second year classes continued what has become a tradition at HMS: the M.D.-Ph.D. summer journal club. There was a particular emphasis this summer on studying papers that utilized novel or paradigmatic approaches or techniques. In particular, a number of the papers studied this summer in the journal club were breakthrough papers, that is papers that resolved longstanding problems or that launched whole new fields of investigation: true “citation classics.” The goal was to use the journal club to discuss some of the different ways of approaching scientific problems utilized in the various subfields of biomedical science. The hope is that students will then take these new approaches back to their own labs, and apply them, perhaps in novel ways, to their own research problems.

The journal club kicked off with a discussion of what has been called the most beautiful experiment in biology, Meselson and Stahl’s demonstration of the semi-conservative nature of DNA replication. In the following weeks, a wide variety of papers were discussed. Work on protein transport, from the laboratory of Jim Rothman, this year’s co-recipient of the Lasker Prize, highlighted the power of biochemical reconstitution in the study of cell biological processes. Molecular biology was the subject of discussion as we examined the work which provided experimental support for the now famous ball-and-chain mechanism of inactivation of certain potassium ion channels. Two successive lively discussions were held on the issue of stem cell research, with one week devoted to the potential of stem cell research for therapeutic medicine and the other week serving as a caveat for those who would rush into stem cell therapies. Continuing with the theme of therapy, we discussed rational drug design, focusing on work towards the development of anti-HIV drugs, from the laboratory of Peter Kim.

The summer journal club was a success in many respects. Attendance was high with approximately half of the combined first and second year classes attending each meeting. More importantly, the discussions were lively, and in true M.D.-Ph.D. form, highly didactic. Given the success of this summer’s venture, the first and second year classes will attempt to carry on the journal club into the school year. The hope is that this endeavor will further allow students to maintain ties to basic science during the first two years of medical school. Journal club will meet on the last Wednesday of each month, in MEC L-007 at 7:15 P.M. All M.D.-Ph.D. students are encouraged to attend. John W. Hanna and Mauro D. Zappaterra are second year M.D.-Ph.D. Program students.

Where are they now?

Harvard M.D.-Ph.D. Program Alumni (n=310) by years of graduation

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*includes 19 in private practice, 6 unknown and 1 deceased

Source: Linda Burnley

30th Anniversary of MARC & MBRS Programs Celebrated

The Annual Biomedical Research Conference for Minority Students was held November 13-17, 2002 in New Orleans, Louisiana. This year marked the 30th anniversary of the Minority Access to Research Careers (MARC) and Minority Biomedical Research Support (MBRS) programs. Over 2500 students gathered for the conference, which represented the largest gathering of research oriented minority undergraduates in the country.

Representatives from Harvard included Linda Burnley (M.D.-Ph.D. Program), Dr. Jocelyn Spragg (Division of Medical Sciences), Dr. James Hogle (chair of the program in biophysics), Michele Jakoulov (administrative coordinator, biophysics), Victoria Love (immunology graduate student) and Jason Sello (postdoctoral research fellow in Biological Chemistry and Molecular Pharmacology, and graduate of the biophysics program).

Juan Carmona, a Summer Honors Undergraduate Research Program (SHURP) student, also won the top award in the cellular biology category for his poster, “Cell-surface Interaction of Transferrin Receptor 1 with the T-cell Receptor and CD3 Signaling Complex in T-lymphocyte Development.” The poster reflected the research he did over the summer in the lab of Dr. Nancy Andrews, the M.D.-Ph.D. Program Director.
approaches among the student presentations, from Anna Greka’s (Year 5-Neuroscience) studies on ion channels and neuronal differentiation to Yonathan Grad’s (Year 6-BBS) computational approach to identifying micro-RNAs to Thanh Nga Tran’s (Year 7-MIT Chemical Engineering) designs of an electrically-switchable surface monolayer.

The next morning’s student talks continue to showcase even more diverse student research. I’m introduced to some unique animal experiments which include, to a first approximation, chilling mice in the cold room and observing ferrets as they watch television. In practice, James Rhee’s (Year 6-BBS) research on mouse PGC-1a and HNF4a during fasting provides a neat molecular explanation for a metabolic adaptive response. Sohail Tavazoie’s (Year 8-Neuroscience) studies of a ferret’s thalamic response to horizontal stimuli indicate that retinal-thalamic connections are dynamic and changeable during development. The apparent madness to the methods yields fruitful discoveries.

Dr. David Nathan, the keynote speaker, presents a broad view of clinical research from his personal and professional experience. From his own role in shaping health care policy, he charts the trends and changes in scientific research over the past years that accompanied the doubling of the NIH research budget. A statistic about funding success (or lack thereof) for new investigators makes the entire M.D.-Ph.D. student group shudder collectively; as a whole, though, Dr. Nathan paints the picture of a challenging but optimistic future for scientific research. He describes the story of one of his own long-time patients, and how this patient’s therapy has evolved with progressing scientific and pharmacologic knowledge.

The afternoon is full of October cold and rain, but that doesn’t keep people from playing golf, going hiking in the White Mountains, and exploring Waterville Valley during the free time. In the evening, everyone reconvenes for the traditional lobster bake and a festive mix of dancing-talking-pool playing-World Series watching-socializing. Somewhere between Shakira and Eminem (informal verdict: genius) the first and sixth year M.D.-Ph.D. classes lead the way on the dance floor, and the fanfare lasts well into the night.

The next morning, we’re driving home on I-93 back to Boston. We stop off at the Hawaiian Isle II, a campy-looking restaurant on the outskirts of Concord. At the 1999 retreat, Rebecca and I had stopped here on the way home, and were charmed by the faux-Polynesian cocktails, typo-ridden Chinese Zodiac placemats and stale fortune cookies. The Hawaiian Isle II stopover has been our retreat tradition ever since.

We’re sitting around the table, and Rebecca mentions how the M.D.-Ph.D. retreat is that one time in the year when you get to gather with everyone in the program and meet all the new students. While preserving its founding ideals, the retreat has grown and evolved from its beginnings twenty years ago; I wonder, as I crack open this year’s fortune cookie, what it will look like twenty years from now.

Bryan K-H. Sun is a fifth year M.D.-Ph.D. Program student (Holmes, DMS, BBS-Genetics).

SAVE THE DATE!

April 24-27, 2003

M.D.-Ph.D. Program Revisit Weekend for applicants offered admission
Celebrity Chefs and Knockout Jockeys

by Lilit Garibyan and Onyi I. Iweala

In his welcoming speech to the HMS/HSDM Class of 2006, Dean Daniel Lowenstein remarked that in their exit interviews, graduating medical students consistently reported that the most enjoyable part of their medical school experience was getting to know their classmates. After only four months in the M.D.-Ph.D. Program, we find that the dean’s words ring true.

For example, this summer, through the required M.D.-Ph.D. course for first year M.D.-Ph.D. candidates, we had the opportunity to get to know our classmates fairly well. While we enjoyed our interactions in the classroom, the most intriguing part of our summer experience was coming to realize the depth and diversity of our classmates’ experiences prior to their arrival at HMS. Collectively, the 11 M.D.-Ph.D. students represent several different countries including Armenia, India, Iran, Israel, Korea, Mexico, Nigeria, and the United States. What is more, as our short autobiographies below reveal, we have strong academic research backgrounds and diverse research interests.

Even though we’ve entered our respective medical school curriculums (seven of us are in the Health Sciences and Technology (HST) while four of us are following the New Pathway), we still maintain close ties with each other. For instance, under the direction of Kush Parmar, we have started the “Kush Parmar’s Celebrity Chef Series.” This dinner club allows us to get together every Tuesday evening to enjoy meals prepared by one of our own classmates.

We recognize the importance of establishing firm bonds with our M.D.-Ph.D. classmates. After all, two years from now, we’re going to have to help each other make the transition from medical school to graduate school. Furthermore, the relationships we build now will serve us well in the future.

This is how our classmates describe themselves:

**Divya Bolar** graduated in 2000 from Johns Hopkins University with degrees in Biomedical Engineering and Electrical Engineering. For the last two years, Div has been engaged in cardiac and pulmonary functional MRI research at the University of California, San Diego. At HMS, Div plans to focus on neuroimaging for his graduate studies. He is specifically interested in using novel MRI imaging paradigms to explore task-based brain activity. Outside of school, Div’s interests include international travel, surfing, teaching, playing guitar, and attending live concerts.

**Sarah Henrickson**, a 2001 graduate of Harvard College, joined the M.D.-Ph.D. Program hoping to combine basic research and clinical medicine. Past research included topics from environmental science to biophysics and immunology, which basically means she hasn’t quite settled on a field yet, but is enjoying trying different things. She spent the last year at NIH, studying cancer using DNA microarrays and planning her wedding. She hopes to find a project that combines exciting techniques and basic science with clinical and biotechnological applications.

**Kush Parmar** graduated from Princeton in 2002 with a degree in molecular biology. His parents are from India, but he was born in New Jersey. When he was one year old, his family moved to Veracruz, Mexico and they have lived there ever since. His interests include art history, anything medieval, flamenco guitar, and international development. One of his biggest commitments is running a non-profit organization (the Cruz Blanca Initiative) that undertakes sustainable development projects in rural areas of Veracruz. He’s thrilled to be here and meet all the amazing personalities that make up the M.D.-Ph.D. community, and he looks forward to a fun experience.

**Marlys Fassett**, a native of Wisconsin, studied biochemistry as a student at Harvard College. In her undergraduate research, she examined the interaction between signaling and membrane microdomains during immune cell recognition. Apart from school, Marlys enjoys performing chamber music, cooking for friends, and reading literature. She hopes to complement her HST M.D. with a Ph.D. in either immunology or developmental biology.

**Onyi Iweala** is a 2002 graduate of Harvard College, where she received an A.B. in Biochemical Sciences. Her undergraduate research centered on the effect of parasitic infections on the immune response to oral vaccines. She is quite excited about the New Pathway curriculum, but is worried that she may be suffering from thoracic outlet syndrome from toting Moore’s *Clinically Oriented Anatomy* around in her backpack one too many times. Onyi hopes to contribute to efforts to improve access to preventive medicine and primary care for underprivileged populations. Her first hand exposure to the challenges of drug and vaccine delivery in Cambodia and Nigeria has spurred her interest in research centered on developing drugs or vaccines that are inexpensive and easy to administer to people in the developing world.

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**The M.D.-Ph.D. Program Newsletter**
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This newsletter is published twice a year. Comments and ideas are welcome.

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Harvard M.D.-Ph.D. Program Newsletter
Ph.D.s Completed

Sandeep Robert Datta, Castle, BBS-Microbiology and Molecular Genetics (DMS) at Harvard University [Michael Greenberg, Ph.D.] Coupling Growth Factors to the Apoptotic Machinery: Biochemical and Genetic Elucidation of the PI-3-Kinase/Akt/BAD Survival Signaling Cascade (8/02).

Anna Greka, Health Sciences and Technology, Neuroscience (DMS) at Harvard University [David Clapham, M.D., Ph.D.] TRP Channels and the Cytoskeleton: Implications for Neuronal Growth and Cellular Motility (10/02).

Chao-Wei Hwang, Health Sciences and Technology, Engineering Sciences, Medical Engineering & Medical Physics at Massachusetts Institute of Technology [Elazer Edelman, M.D., Ph.D.] Local Pharmacokinetics of Stent-Based Drug Delivery (5/02).

Rahul Manu Kohli, Health Sciences and Technology, BBS-Biological Chemistry and Molecular Pharmacology (DMS) at Harvard University [Christopher T. Walsh, Ph.D.] Macrocyclization Catalysis by Excised Thioesterase Domains from Natural Product Synthetases (11/02).

Gisela Maria Rodriguez Sandoval, Health Sciences and Technology, Neuroscience (DMS) at Harvard University [Gary Ruvkun, Ph.D.] Molecular Genetic Analysis of an Interaction between the Vesicular Acetylcholine Transporter and Synaptobrevin in Caenorhabditis Elegans (7/02).

Celebrity, from page 5

Lilit Garibyan graduated from UCLA in 2001 with a degree in Microbiology and Molecular Genetics. She was born in Armenia but at age twelve she moved to California with her family and has been living there ever since. At UCLA her research mainly focused on bacterial genetics. Lilit loves to teach, play basketball and talk about Armenian people. Her favorite virus is KSHV, her favorite molecule is DNA and her favorite book is “The Double Helix” by James D. Watson. In the future she hopes to work at a university where she can teach, attend to patients and maintain her own research laboratory.

Jubin Ryu graduated from Stanford in 2001 with degrees in English and Biological Sciences. He is interested in defining mechanisms behind cognitive processes such as learning and memory using molecular, biochemical, and electrophysiological tools. In the future, he hopes to integrate basic science research with clinical and teaching duties.

Scott Vafai graduated in 2002 from Princeton University with a degree in molecular biology. As an undergraduate, he conducted research on the molecular basis of Alzheimer’s Disease. Scott is currently in the HST program and plans to do his Ph.D. in the neuroscience program.

Marc Wein joins the M.D.-Ph.D. Program in the New Pathway after graduating from Yale University in 2002 with a BS/MS degree in Molecular, Cellular, and Developmental Biology. Marc’s research background is in signal transduction, in the context of behavioral neuroscience and inflammatory responses. In his graduate work, Marc intends to apply knowledge of basic mechanisms of signaling to the study of lymphocyte development and differentiation, hoping to gain insight into the cell biology underlying disorders such as autoimmune diseases and hematopoietic neoplasias. Marc’s favorite anatomical structures are the thoracic duct and the left recurrent laryngeal nerve.

Sonia Cohen graduated from Johns Hopkins with an undergraduate degree in systems neuroscience before joining HST this fall. In her previous research at Hopkins she studied the role of the transcription factor CREB in mediating sympathetic nervous system survival and growth. Sonia is interested in continuing to study signal transduction – especially regulatory mechanisms that influence differential transcription, but is also exploring other areas of research.

Ruth Foreman is coming from Philadelphia, Pennsylvania where she studied biochemistry and the history and sociology of science at the University of Pennsylvania. While there she was involved in musical theater. For the past year she worked in developmental biology at Penn’s Medical School studying the role of a gene (Fodx3) in early mouse embryogenesis. She was also known to moonlight as a yoga and Pilates teacher (and student).

Program Briefings

Student Receives Award
Congratulations to M.D.-Ph.D. Program student Michelle Lee who was recently selected as the William and Charlotte Cadbury Scholar by the National Medical Fellowships, Inc. This award is “presented annually to a senior, underrepresented medical student in recognition of outstanding academic achievement, leadership, and community service.” She traveled to the AAMC Conference in San Francisco to receive the award.

Staff Update
Welcome Jennifer Au-Yeung who joined the office in September as the new staff assistant. Jen graduated from Boston University in 2002 with a B.A. degree in Economics.

Alumni Readers
Update your contact information by emailing any changes to mdphd@hms.harvard.edu. Story ideas for the newsletter are always welcome.
For the Record

Recent Publications


*Equal contributors.
For the Record

Incoming M.D.-Ph.D. Students, 2002-2003

Divya S. Bolar of Martinsville, NJ graduated from Johns Hopkins University in 2000 with a BS in Biomedical Engineering, Electrical Engineering.

Sonia Cohen of Kenilworth, IL earned a BA in Neuroscience from Johns Hopkins University in 2002.

Marlys S. Stempihar Fassett of Beloit, WI graduated from Harvard College in 2001 with an AB in Biochemical Sciences.

Ruth K. Foreman of Harrisville, PA completed a BA in Biochemistry, History and Sociology of Science from the University of Pennsylvania in 2001.

Lilít Garibyan of Glendale, CA graduated from UCLA in 2001 with a BS in Microbiology and Molecular Genetics.

Sarah E. Henrickson of Takoma Park, MD received an AB in Biochemical Sciences from Harvard College in 2001.

Onyinye I. Iweala of Potomac, MD graduated from Harvard College in 2002 with an AB in Biochemical Sciences.

Kush M. Parmar of Boca del Rio, Veracruz graduated from Princeton University in 2002 with an AB in Molecular Biology.

Jubin W. Ryu of Morgantown, WV earned a BA/BS in English/Biological Sciences from Stanford University in 2001.

Scott B. Vafai of Edison, NJ received an AB in Molecular Biology from Princeton University in 2002.

Marc N. Wein of Cheshire, CT graduated from Yale University in 2002 with a BS, MS in Molecular, Cellular and Developmental Biology.

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