Reality Check for Bench to Bedside
by Sarah Henrickson

At each interview for M.D.-Ph.D. programs, we were all asked the same question — is it possible to combine a successful academic career while caring for a patient population? Before the conference, I had barely begun my second semester of the HST program and was so overwhelmed with new information and endless research opportunities I was beginning to doubt I’d be able to do either one — let alone both! Attending the “Days of Molecular Medicine” symposium in San Diego in March, hosted by UCSD, The Salk Institute and Nature Medicine was a reality check for me. Not only is it possible to treat patients and do cutting-edge research, but there is also a huge community of people who are excited to discuss how they do it and give advice to current students.

The conference began with a keynote address from my former group leader, Tom Waldmann (NIH), on a career that has involved both fascinating discoveries in basic science related to IL-2 and IL-15 as well as clinical trials aimed at treating previously untreatable patient populations. His discussion of the recent success of monoclonal antibodies in treating a wide variety of disorders began the weekend’s wide-ranging exploration of exciting new (and future) immunotherapies.

The first session focused on cell-based therapies and included an intriguing talk by Harvard’s own Megan Sykes on the potential for mixed hematopoetic chimerism in the treatment of hematopoetic malignancies and the induction of transplantation tolerance.

Reminiscences of an Octoannarian
by Finny Kuruvilla

The greatest scholar of our time in biblical Greek, Professor Bruce Metzger of Princeton University, wrote a book in his eighties entitled Reminiscences of an Octogenarian. There he reflected on his life and scholarly pursuits. Though this article is miniscule in comparison to his book, my title is inspired by his title. While “octoannarian” is not a real English word, I take it to mean “eighth year.” As I am now completing my eighth year and ready to graduate, I find myself reminiscing about my own training and the many lessons I have learned. Reflecting on my years in the M.D.-Ph.D. Program, I would like to offer four pieces of advice to junior students:

1. Develop an independent intellectual life outside the lab. The main transition that we make from our undergraduate to graduate years should be one of independence. As undergraduates, we were mostly doing research projects that other people devised. As graduate students, we find ourselves developing original ideas and then carrying them into experiment. However, there is a natural trap that we can fall into, particularly two to three years into a Ph.D., which is simply that of doing the next obvious experiment. If we find ourselves in that state, then we will, in a sense, not be much higher than we were as undergraduates since we are not using our intellectual creativity. A remedy for this is to cultivate an independent intellectual life outside the lab. We are blessed to be at Harvard and MIT because there is so much happening here in so many different fields. I found myself taking extra courses at MIT in a field very different from my Ph.D. work, and I thoroughly enjoyed it. It provided me the opportunity to be engaged in a field outside my lab work and

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has given me ideas for future research. I strongly believe that this intellectual independence is important in order to balance the consequences of focusing on a very small field, as we naturally do as Ph.D. students.

2. Be humble. Most people begin their M.D.-Ph.D. programs with lofty notions of making grand contributions to a field, perhaps even dreaming to revolutionize it. It is certainly healthy to dream, as it inspires us to work hard and be creative. However, it is just as important to temper our dreams with humility.

My Ph.D. advisor once said in a lab meeting that when you’re doing good science, around 90% of what you’re doing either won’t work or won’t lead to publication. That thought is certainly sobering. While I feel that I had a successful Ph.D., in looking back at my old lab notebooks, I think it probably is true that 90% of what I did never got published but will probably languish away on a shelf where no one will ever read it. Though I certainly learned a great deal, even in failed experiments, I think it’s especially important to be humble given the fact that much of science does not lead to tangible benefits to society. In the chemistry department where I did my graduate work, one of the premier departments in the country, I was told that of the thousands of papers to come out of the department, only a small handful actually influenced how people synthesize drugs or provided a boost to the “real-world” pharmaceutical and chemical industry. This should not be surprising, since science is not necessarily about practical applications, but we must be honest and humble in acknowledging this to ourselves.

Lest we think this humility should be confined to science and not medicine, I was reminded of similar truths on the wards. For example, I am reminded of a patient from my internal medicine rotation who was suffering from a severe COPD flare. After days of our heroic efforts, including intubation and intravenous steroids, she improved and was discharged. The next day she was readmitted because she smoked again and precipitated another flare. Feeling somewhat discouraged that our medical team was merely a glorified bandage, I learned the valuable lesson that medicine really only addresses a fraction of human problems — that should also make us humble.

This past January I was in India where I had the opportunity to spend time with many different capacities. In the midst of receiving congratulations on being nearly finished with eight years of hard training, I was struck by how much good I saw people with much less education doing to help their neighbors. Could I be sure that my publications, involving much more money spent, would really help someone as much as those people would? Even in our best discoveries published in prestigious journals as we clone genes, identify phosphorylation sites, dissect pathways, and find disease markers, we have to keep our accomplishments in perspective. While not a cause for discouragement, it should certainly be a reminder of humility.

3. Use the retreats as a resource. The M.D.-Ph.D. retreats are, in my estimation, the glue of the program. In my eight years here, I attended all eight retreats. Sometimes it was difficult to attend because of heavy classroom duties, being busy in the lab, or a call schedule in the hospital, but it was always worth it. Besides the great food and the beautiful setting, the retreats bring together students of all years as well as junior and senior faculty. Because the retreat participants are a “captive audience,” away from emails, the lab, and the hospital, retreats present the opportunity to have probably the most relaxed conversations you will have about research, the hospital, and life outside of academia. The key to using a retreat is to see it as more than an opportunity to have fun with your friends (although it certainly is). Retreats provide a unique opportunity to meet many interesting people further along in their training who can be a tremendous resource to you for knowledge and perspective. Finally, retreats might be the very best way to put what you are doing in context and gain a sense of the bigger picture, as it relates to academia as well as your own training.

4. Be bold. Michael Crichton, well known for his books such as Jurassic Park, graduated from Harvard Medical School in 1969. Though he was not an M.D.-Ph.D. student, he shared something that we have — a passion for two fields. He enjoyed medicine but also loved to write. Interestingly, he did something that many M.D.-Ph.D.’s do — he chose a postdoctoral fellowship over a residency. So Crichton moved from Boston to the West Coast and did research at the Salk Institute in La Jolla, California. There he had the opportunity to interact with Jonas Salk, by that time already well known for his work on the polio vaccine. Crichton was deeply feeling the pressures of a dilemma between a passion for writing and the prestige of being a successful doctor. But it was Salk who told him, “fame was a complete load of nothing.”

“It is certainly healthy to dream... However, it is just as important to temper our dreams with humility.”

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Annual Spring Dinner for the M.D.-Ph.D. Class of 2003

The M.D.-Ph.D. Program’s Annual Spring Dinner was held on May 12. Dr. Malcolm Cox, the incoming Dean for Medical Education, offered a toast to the graduates and graduating M.D.-Ph.D. student Finny Kuruvilla offered closing remarks (see article, page 1).

(Clockwise, L-R) Alex Carter and his advisor, Dr. Rosalind Segal; Michelle Lee, Jeffrey Lin, Sarah Pak, and Dr. David Golan; Channing Yu and his advisor, Dr. Stuart Orkin; Dr. Malcolm Cox, Dr. Nancy Andrews, and Anna Farago; Cynthia Wu, Irwin Lee and daughters Aurora and Cassia.
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There was also a great talk by Ralph Steinman (The Rockefeller University) discussing the use of dendritic cells with exciting methods for targeting antigens directly to these great T cell activators, allowing doctors to load these T cell activators with the necessary antigens to target diseased cells more efficiently. The second session focused on antibody-based therapies with a focus on monoclonal antibodies. Mark Sliwkowski (Genentech) discussed the role of Herceptin for treatment of certain forms of breast cancer. The third session focused on co-stimulatory molecules, with great talks by Arlene Sharpe (Harvard) on the new members of the B7/CD28 family and the importance of the balance between regulatory T cells and effector T cells in inducing transplantation tolerance and cancer therapy. A fourth session involved cytokines with Peter Libby (Harvard) forming one part of a triad of atherosclerosis lectures (including Joseph Witzum of UCSD and Goran Hansson of the Karolinska Institute). These lectures were spread throughout the conference; they discussed everything from prevention by way of vaccination to the importance of inflammation to potential uses for anti-inflammatory prostaglandins (like PGE2) as therapy. The last session was more diverse and included DNA/RNA/Peptide therapies, with a intriguing talk by Wadhi Arap (MD Anderson Cancer Center) on the use of “cell panning” and antibody panning to look for peptides expressed in tumors, as well as proapoptotic peptides, for uses including destruction of angiogenic vasculature in neoplasms.

The conference also offered students opportunities to interact with faculty through poster presentations and selected oral presentations. The conference was fairly small, which allowed for opportunities to talk with the leaders in immunology over a bagel at the amazing Salk Institute (right on the cliffs over the Pacific) or while peering at seahorses at the Birch Aquarium. The Physician-Scientist forum this year focused on the “Translational Medicine make the future both terribly unclear and terribly exciting. In this world, advice gives to aspiring writers is this: “the first step is to stop asking for advice.” While I think this could be construed as hubris, and doubtless would be with the wrong attitude, there is an element of truth in his words. The host of new technologies in science and medicine make the future both terribly unclear and terribly exciting. In this world, advice will only go so far because no one really knows how things will shape out. This does not mean that we should not learn from each other, and not spend time understanding each other’s experiences (in places like the retreats). Yet it does mean that we must not uninspiredly copy the pattern of what has worked for someone else. Those who follow their own dreams find the greater success.

For those of us graduating in 2003, I believe we are at the most exciting time in the history of science and medicine. Disciplines are melding at an astonishing rate to answer questions in biology that we never before could approach. We are indeed fortunate to be trained at an institution and part of this M.D.-Ph.D. Program with so many strengths in different fields and so laden with resources. Thus, I could summarize my main reminiscence in one word: thankfulness.

Sarah Henrickson is a second year M.D.-Ph.D. Program student (HST, DMS-Immunology).

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Crichton decided not to be a clinician and to pursue writing, a decision he says that people around him likened unto “quitting the Supreme Court to become a bail bondsman.” Years later, it was apparent that Crichton’s choice was the right one for him. As M.D.-Ph.D.’s, we have different passions and our paths will surely be different. But I hope that they will be marked by a similar sense of boldness.

One piece of advice that Crichton gives to aspiring writers is this: “the first step is to stop asking for advice.” While I think this could be construed as hubris, and doubtless would be with the wrong attitude, there is an element of truth in his words. The host of new technologies in science and medicine make the future both terribly unclear and terribly exciting. In this world, advice will only go so far because no one really knows how things will shape out. This does not mean that we should not learn from each other, and not spend time understanding each other’s experiences (in places like the retreats). Yet it does mean that we must not uninspiredly copy the pattern of what has worked for someone else. Those who follow their own dreams find the greater success.

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Finny Kuruvilla is an eighth year, graduating M.D.-Ph.D. Program student (HST, GSAS, Chemistry). This article is taken from his closing remarks delivered on May 12, 2003 at the M.D.-Ph.D. Spring Dinner.

The M.D.-Ph.D. Program Newsletter Volume 14, No. 1

Editor
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This newsletter is published twice a year. Comments and ideas are welcome.

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Director
David E. Golan, M.D., Ph.D.
Co-Director
Linda Burnley
Director of Administration & Finance
Yi Shen
Senior Financial Analyst
Robin Lichtenstein
Admissions Specialist
Meet Dr. Joel Hirschhorn. Joel joins the program’s Committee of Advisors (COA) in a new role created to advise medical students who are motivated to pursue a Ph.D. degree but are not yet admitted to a Ph.D. program. The appointment of Dr. Hirschhorn to this special role fills a void that has existed for medical students who need advice about whether to pursue Ph.D. education and, if so, what the optimal path would be to maximize the opportunities. For example, M.D.-only students who matriculate here with an interest in combining medical and graduate studies may not have regular access to the advising resources that are available to M.D.-Ph.D. matriculants. Since M.D.-Ph.D. students have the advantage of a network of resources and advice from the M.D.-Ph.D. Program, Drs. Nancy Andrews and Alan Michelson, co-chairs of the COA, decided to make similar advising resources available to medical students interested in combining both the M.D. and Ph.D. degrees.

The program’s Committee of Advisors has the responsibilities of advising students on their academic programs, monitoring their progress, and formulating strategies for dealing with any academic or personal issues that may arise. Members include designated M.D.-Ph.D. advisors for each of the five Harvard Medical School Societies. The COA meets approximately three times each year as a full group.

Joel graduated from the Harvard M.D.-Ph.D. Program in 1995 and did his Ph.D. thesis work with Fred Winston, studying yeast genetics and chromatin structure. He completed clinical training in Pediatrics and Pediatric Endocrinology at Children’s Hospital in Boston, and did his postdoctoral research training with Eric Lander at the Whitehead/MIT Center for Genome Research. Joel is currently an Assistant Professor at Children’s in the Harvard Medical School Department of Genetics, where he works on the genetics of common disease and complex traits in humans. He also maintains a presence at the Whitehead/MIT Center for Genome Research as Director of Endocrine Genetics and remains clinically active as an attending in Pediatric Endocrinology at Children’s.

Dr. Harold Amos

Members of the M.D.-Ph.D. Program family are among the countless individuals affected by the death of Dr. Harold Amos on February 26, 2003, several days after suffering a stroke. He was 84. He was teacher, advisor, and mentor to generations of HMS students and DMS graduate students.

Dr. Amos was a graduate student and then, for close to 50 years, a faculty member in the Department of Bacteriology and Immunology (now Microbiology and Molecular Genetics) at Harvard Medical School, where he was named Maude and Lillian Presley Professor of Microbiology and Molecular Genetics in 1975 and became emeritus in 1988. He was known for his work on bacterial metabolism, virology, and animal cell culture, and his scientific publications cover the years from 1953 to the mid-'80s. After his official retirement from administrative positions, he continued to derive much satisfaction from doing experiments in the laboratory and thinking about scientific questions.

As chair of his department from 1968 to 1971, and again from 1975 to 1978, Dr. Amos was known particularly for his interest in and encouragement of students and young faculty. The door to his office was almost always open, and he welcomed drop-in visitors. He was an effective and tireless supporter of all students, especially members of under-represented groups, in science and medicine, and served on numerous boards and advisory committees dedicated to these efforts.

Dr. Amos received many important awards that recognized both his scientific accomplishments and his devotion to educational initiatives and the welfare of students. These include honorary doctoral degrees from Harvard University and from his alma mater Springfield College, the Centennial Medal of the Harvard Graduate School of Arts and Sciences, the first Dr. Charles Drew World Medical Prize from Howard University, and the Public Welfare Medal of the National Academy of Sciences. A modest man, few of his colleagues knew the full range of honors he had received.

Above all, Dr. Amos is remembered for caring deeply about people, and was friend, teacher, advisor, mentor, colleague, role model, inspiration, and confidante to hundreds if not thousands of people of all ages, and from all backgrounds and stations in life.

A service of music and remembrance in celebration of Dr. Amos’s life was held at the American Academy of Arts and Sciences, of which he was a member, in Cambridge, Massachusetts on Friday, May 16.
For the Record

**Ph.D.s Completed**

Francis J. Alenghat, Health Sciences and Technology, Biophysics (GSAS) at Harvard University [Donald Ingber, M.D., Ph.D.] Mechanotransduction Through Integrins (5/03).

Andrew E.H. Elia, Health Sciences and Technology, BBS-Cell Biology (DMS) at Harvard University [Lewis Cantley, Ph.D.] Proteomic Screen Reveals that the Polo-box Domain is a Phosphoserine/threonine-binding Module (5/03).


Hien Thanh Tran, Health Sciences and Technology, Neuroscience (DMS) at Harvard University [Michael Greenberg, Ph.D.] A Role for Forkheads in the Response to Stress (6/03).

Victoria Wang, Health Sciences and Technology, Biology at Massachusetts Institute of Technology [Phillip Sharp, Ph.D.] Investigating the Role of Oct-1 in Development and Lymphopoiesis (5/03).

**Program Briefings**

The M.D.-Ph.D. Program extends a warm welcome to the incoming Dean for Medical Education, Dr. Malcolm Cox.

**2003-04 Admissions Process Update**

The M.D.-Ph.D. subcommittee on admissions reviewed 430 (56% men; 42% women) applications from undergraduates applying for admission to the M.D.-Ph.D. Program. Ten applicants (6 women; 4 men) accepted offers to matriculate at HMS: Hannah Chang (Princeton), Christy Comeaux (Johns Hopkins University), Salil Garg (University of Chicago), Thomas Hocker (Yale University), Peggy Hsu (Princeton University), Ilya Leskov (Swarthmore College), Ken Lin (Stanford University), Mariah Mason (University of Colorado-Boulder), Marissa Wagner (Yale University), and Narie Yoo (Harvard University). *Note: The following students, who deferred admission in 2002, will also matriculate in 2003-04: Rachel Bortnick (University of Chicago), Vijay Sankaran (University of Pennsylvania) and Ram Srinivasan (Caltech).*

**New Presidential Scholarship Funds International Student**

The M.D.-Ph.D. Program has named Hannah Chang as the recipient of the new Presidential Scholars award. This award was recently established by Harvard University President Lawrence H. Summers to ensure that the most talented international students are able to come to Harvard to prepare for careers in academic medicine without assuming undue financial burdens. As part of this new funding opportunity, which is currently offered in eight of Harvard’s graduate and professional schools, President Summers has approved funding for one international M.D.-Ph.D. student matriculating in 2003-04. Ms. Chang, a 2004 Princeton undergraduate from Taiwan, ranked as one of the top 10 out of 430 M.D.-Ph.D. applicants, and will join the new class in July.

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**SAVETHEDATE!**

October 24-26, 2003

M.D.-Ph.D. Program
21st Annual Retreat
Waterville, New Hampshire

**Revisit Luncheon, April 25, 2003**

(L-R) Anna Farago, Savita Dandapani, Rebecca Spencer, Yonatan Grad, and incoming students Kenny Lin and Marissa Wagner at the M.D.-Ph.D. Revisit Luncheon. Affiliated faculty members, current M.D.-Ph.D. students, and potential incoming students gathered for lunch to discuss studying at Harvard. Incoming students also spent much of the afternoon meeting with potential summer lab mentors.
For the Record

Recent Publications


Kim do H, Sarbassov DD, Nauli SM, Catapano LA, Mar;129(6):1435-42. BDNF stimulates migration of cerebellar granule cells.


Class of 2003 Appointments

Alexandre R. Carter, Neurology, Washington University, St. Louis, MO.

Lisa A. Catapano, Psychiatry, George Washington University, Washington, DC.

Tammy Chang, Surgery, UCSF, San Francisco, CA.

Benjamin E. Gewurz, Internal Medicine, Beth Israel Deaconess Medical Center, Boston, MA.

Heather L. Hinds, Preliminary Medicine, Stanford University Programs, Stanford, CA; Neurology, UCSF, San Francisco, CA.

Eugene Y. Koh, Orthopedic Surgery, Rhode Island Hospitals/Brown University, Providence, RI.

Finny G. Kuruvilla, Pathology, Brigham and Women’s Hospital, Boston, MA.

Mykol Larvie, Preliminary Medicine, Radiology, Massachusetts General Hospital, Boston, MA.

Benjamin S. Leader, Emergency Medicine, Rhode Island Hospitals/Brown University, Providence, RI.

Irwin H. Lee, Radiation Oncology, University of Michigan Hospitals, Ann Arbor, MI.

For the Record

Sohail F. Tavazoie, Internal Medicine, Brigham and Women’s Hospital, Boston, MA.

Michelle A. Lee, Pediatrics, Children’s Hospital, Philadelphia, PA.

Jeffrey P-C. Lin, Preliminary Medicine, Massachusetts General Hospital, Boston, MA; Radiology, Barnes-Jewish Hospital, St. Louis, MO.

Mireya F. Nadal-Vicens, Preliminary Pediatrics, Psychiatry, Massachusetts General Hospital, Boston, MA.

Clark F. Schierle, Plastic Surgery, McGaw Medical Center, NW University Program, Chicago, IL.

Abraha Taddese, Transitional, Alameda Country Medical Center, Oakland, CA; Radiology, Mt. Sinai Medical Center, Miami, FL.

Sohail F. Tavazoie, Internal Medicine, Brigham and Women’s Hospital, Boston, MA.

Kenneth Y. Tsai, Preliminary Medicine, Dermatology, Massachusetts General Hospital, Boston, MA.

David Wu, Pathology, Brigham and Women’s Hospital, Boston, MA.

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