



BBS Bulletin

September/October
2004

Contents

- Alternative Careers .3
- BBS Awards 3
- Community Service 5
- Faculty Profile:
David Rudner 6
- Announcements 7
- Faculty Profile:
David Fisher 8

Editorial Staff

Kathryn Auld
Zeke Bernstein-Hanley
Chris Brown
Laura Burrack
Catarina Campbell
James Cha
Danny Chou
Allan M. Gurtan
Jennifer Kowalski
Nitasha Manchanda
Joan Ruderman
Jennifer Svendsen
Annie Yang

Contributing Authors

Olaia Naveiras Torres-Quiroga
Laura Burrack
Katie Auld
Yao Chen
Jennifer Svendsen
Maria Naylor

A Star is Born: Creating the Harvard Stem Cell Institute

Olaia Naveiras Torres-Quiroga (G3)

Politics, Politics....

“Do you go for Presidential lines or for non-Presidential lines?” This may sound like a question for fashion victims during the upcoming election, but it is the essence of the current human stem cell debate in the United States.

At this moment, using federal funds to perform research on “non-Presidential” human embryonic stem cell lines (that is, any stem cell lines not among the pre-existing lines approved for research use by President Bush) constitutes a felony punishable by a minimum of 10 years in prison and a \$1 million fine. While the Clinton administration allowed human embryonic stem (ES) cell research as long as the stem cell lines were derived with private funds, President Bush and his administration took a more ethically conservative stance and restricted federal funding exclusively for research on human ES cell lines derived before August 9th 2001. At the time the decision was made, these 78 so-called “Presidential lines” were thought to be both

easily accessible to researchers and sufficient to determine the potential of stem cell therapies in the cure of degenerative diseases. Unfortunately, it is now known that (i) only 19 of these 78 ES lines are actually available for distribution, (ii) they are accumulating genetic abnormalities due to extensive culturing, and (iii) the fact that they were co-cultured with mouse fibroblasts makes them unusable for human clinical trials.

Luckily for the future of U.S. stem cell research, Harvard visionaries Douglas Melton and Andrew McMahon foresaw the limitations of the Presidential lines and, in 2001, used private money to develop new high quality human ES cell lines. Seventeen of these cell lines were published in March and soon will be widely available thanks to Howard Hughes Medical Institute funds. Still, very few U.S. investigators will be eligible to perform research with these non-Presidential lines because the majority of researchers rely, at least in part, on federal grant support.

see ‘Stem Cell’ on page 2

atggacttacggcatgcatgtttgacggcgcgatccagttgaccagttgaccagtttagggcaaatatataatgcacagatcagcatgacttacggcatgacttacgacttacgatgacttacggcgcgatgcatgtttgacggcgcgatccagttgaccagtttagcaaatatataatg

2003 DMS Student Survey

Laura Burrack (G3)

A year and a half ago, DMS students were invited to complete a lengthy survey covering a variety of topics including general student satisfaction, faculty mentoring, and administrative issues. The survey data was never released to the DMS community leaving some of us on the BBS Bulletin staff (and likely many of the BBS Bulletin readers) to wonder what happened to the collected information. Specifically we wanted to know what was learned and how it was used to inform faculty members and program directors about student thoughts and needs as they make administrative and academic decisions. I recently talked with Tom Fox, the Associate Dean for Graduate Education, about the DMS survey to find out a

bit more about the original goals of the survey and what was done with the knowledge gained from it.

The survey originated from a desire for formal student input in reviewing the current DMS programs and determining the future directions of graduate education at the medical school. The committee responsible for the survey was a group of faculty members including the directors of each of the four programs within DMS, and it included Bob Kingston, who subsequently became the new director of BBS. All current DMS students were asked to complete the on-line survey. Approximately 230 students responded to most or all of the survey

see ‘DMS Survey’ on page 3

A Sad State of Affairs

Currently, three years after the institution of President Bush's stem cell policy, the state of stem cell research in this country continues to lag behind its potential, as well as behind the continued advances of other nations. Where, at one time, the National Institutes of Health had anticipated the use of federal funds to perform research on ES lines privately derived from some of the 400,000 frozen embryos awaiting disposal at fertility clinics across the country, now many researchers avoid human ES research fearing greater restrictions on their future work. Here in the U.S., while 150 million potential candidates for stem cell therapies wait for news from Congress on the stem cell ban, embryonic stem cell research is rapidly advancing worldwide. In fact, just last March Shin Yong Moon's group in South Korea developed the first human ES cell line derived from a cloned blastocyst, demonstrating that somatic cell nuclear transfer (known before as therapeutic cloning) is possible in humans. The question remains as to how the U.S. can stay at the top of the stem cell community when the restrictions on this field are so great and the scientific questions so challenging.

Hope Springs Eternal – The Birth of the Harvard Stem Cell Institute

In response to this research crisis, several major U.S. initiatives have been created to allow for the continued study of the therapeutic potential of human embryonic stem cell research and to ensure non-federal funding when the use of non-Presidential lines is involved. Several states, including New Jersey and California, have or are considering legislation to provide private funding to promote continued stem cell research. While Massachusetts has yet to join the pro-stem cell community at the level of state legislation, Harvard is walking several steps ahead in the fight.

On April 23, 2004, the creation of the Harvard Stem Cell Institute (HSCI) was announced. Two main purposes brought the project together. The first is to gather efforts in a unified forum from multiple disciplines involved in studying the ethical, political, economic, and scientific issues inherent to ES cell research. The second goal is to promote increased collaboration among the already world renowned Harvard stem cell scientists in the hope that more progress could be made through collaboration than through competition. To meet these goals, the HSCI has successfully involved seven Harvard schools in the project: the Medical School, the School of Public Health, the School of Arts and Sciences, the Law School, the Business School, the Divinity School, and the Kennedy School of Government. Since the Institute must be privately funded in order to perform research on or to develop any new ES lines, a \$100 million fund-raising campaign has been launched with full support of Harvard University President, Lawrence Summers.

With regard to the scientific work of the Institute, five

pathologic conditions have been targeted as the initial research focus: diabetes, blood diseases, neurodegenerative diseases, cardiovascular diseases and musculoskeletal diseases. Each project funded by the HSCI will have to be approved by a mixed committee of scientists and ethicists. Co-directors Doug Melton (GSAS) and David Scadden (MGH) are also committed to ensuring that the research produced through the HSCI will eventually be used clinically to treat as many diseases as possible. Ultimately, collaborative efforts must merge to answer the one common question on human stem cell research: how to differentiate embryonic stem cells into specific tissues that can be used for the cure of these target diseases. There are currently 25 participating Harvard stem cell labs, 13 of which are affiliated with the BBS Program and listed below. To promote a sense of community and communication among these labs, joint seminars are held on a monthly basis. In addition, an annual symposium is planned to allow for disclosure of new findings to the whole Harvard medical community. No new building for the Institute is planned in the near future, but a new stem cell core facility will allow all researchers both to profit from technical expertise and to assay non-Presidential ES lines exclusively through private funding.

Overall, HSCI truly is a one-of-a kind endeavor uniting researchers from a myriad of disciplines to study a common issue. It is still only the beginning for this institute, and there will definitely be challenging times ahead, scientifically and politically. Many technical problems must be defeated before differentiated tissues from ES cells constitute a widespread therapeutic option for specific diseases, and many ethical issues are still to be raised. In the midst of these issues, a think-tank like the HSCI will be an incredibly valuable resource to find optimal solutions, and it will be exciting to watch the future of this organization unfold.

(More information on the Harvard Stem Cell Institute will be available soon at www.stemcell.harvard.edu)

BBS Stem Cell Laboratories

Spyros Artavanis-Tsakonas
Connie Cepko
George Daley
Niels Geijsen
Gary Gilliland
Ron Kahn
Andrew Lassar
Richard Mulligan
Stuart Orkin
Bruce Spiegelman
Daniel Tenen
Chris Walsh
Len Zon

way to learn more about a career, so ask your lab-mates, classmates, friends, and family if they know anyone in the field you are considering. In fact, part of what is great about being in such a large program is being part of the BBS network... so use it!

2) Fairs and Forums

Another great way to meet people in various careers is to attend the job fairs and career forums sponsored by BBS, DMS, the Harvard Office of Career Services, and the Biotechnology Club (see www.thebiotechclub.org for events). At the fairs, companies and organizations come to Harvard to recruit upcoming graduates for positions, and even if you are not looking for a job yet, the representatives are usually very willing to talk about what they do and what they like about it. Aside from being an effective networking tool, these glimpses into daily life outside the lab environment can introduce you to various career options you may not have considered otherwise.

3) The Office of Career Services

This office is based in Cambridge, and as a result, we are less familiar with it here on Longwood. However, I highly recommend checking out their website at www.ocs.fas.harvard.edu. This office has many resources, events, and counselors to help students through the career search, including everything from personality and interest testing, to job listings and taped mock interviews. There is even a three-session Career Transition Workshop Series specifically designed for GSAS students wondering about options outside academia.

4) Books on Alternative Careers

There is a plethora of career-hunting guides out there, and some of the most widely read general guides are the What Color is Your Parachute? series of books by Richard Nelson Bolles. For a more specific look at some of the non-academic options available to scientists, consult Alternative Careers in Science: Leaving the Ivory Tower, edited by Cynthia Robbins-Roth. This collection of essays by science PhDs is useful for its inside look into the transition from academic science into the worlds of business, publishing, broadcasting, consulting, patent law, public policy, and more. Although this resource is somewhat out-of-date, having been published in 1998, it is still worth reading, if only for the descriptions of daily life outside of the lab.

5) Career Guides on the Web

Once you have decided on a few fields that interest you, how do you find your dream job? In addition to establishing contacts and using the Office of Career Services, you may consult several job-search websites recommended by our alums: www.vault.com and www.wetfeet.com (both general); and www.biospace.com (specific to science jobs). Some of these sites also offer advice for resumes and

interviews, so they can be helpful at all stages of the job search process.

6) Get Involved

A great way to learn about a new field is to become involved in it while still a student. For instance, if you're thinking about getting into business, read the Wall Street Journal; if you want to be a science writer, write for Harvard papers and join the National Association of Science Writers. Joining a professional organization such as the NASW can give you access to job postings and lists of members who might be helpful contacts.

7) Try This On for Size: Facilitated Internships

If you're still hesitant about which direction to go after graduate school, try one of the facilitated internships available through the BBS program. The most popular internships are at AstraZeneca and Cell Press, and there is a list of other affiliates in the BBS office. These paid internships are a great way to try out a different career path for a short period of time, ranging from three to twelve months, while gaining valuable experience to add to your resume.

8) Begin Early

In conclusion, deciding on a post-graduate career will take research and soul-searching. According to the Harvard Office of Career Services, there are several phases of the process: self-assessment, career exploration, and the job search. In other words, to get the best results from your job search, you will need time to figure out what interests you. Therefore, as one of our alums advises, the most important resource is time: Plan enough time for the process and you'll likely be happier with the outcome!

Helpful Career Planning Resources

Harvard Office of Career Services

54 Dunster St, Cambridge

Websites

www.ocs.fas.harvard.edu

www.thebiotechclub.org

www.vault.com

www.wetfeet.com

www.biospace.com

Books

What Color Is Your Parachute? 2004: A Practical Manual for Job-Hunters & Career-Changers by Richard Nelson Bolles

Alternative Careers in Science by Cynthia Robbins-Roth
So What Are You Going to Do With That?: A Guide for M.A.'s and PhD's Seeking Careers Outside the Academy by Susan Basalla and Maggie Debelius (Out-of-print, but still available used or at libraries)

Ethos- Longwood Area/ JP

Help low income elders in the greater boston area stay at home and remain independent for as long as possible. Also serves LGBT elders.

Brookline School-Community Partnership- Steps to Success(STS)- Longwood Area/Brookline

Tutor teens, grades 7-11 from low-income families in Brookline.

Home For Little Wanderers-Longwood Area

Work in various programs that focus on the healthy development of children at risk, their families and communities.

Food For Free-Cambridge

Help prevent local hunger by rescuing fresh foods that might otherwise go to waste and distributing them within the emergency food system.

Prevention NOW!, Inc- AAA School Age Child Care Program-Longwood Area/ JP

Work with others to provide comprehensive and innovative services that meet the educational, recreational, social, health and vocational needs of modern urban youth.

MissionSAFE: A New Beginning, Inc.- Longwood Area/ Mission Hill

Tutor and/or mentor primarily African-American and Latino adolescents from low-income and at-risk neighborhoods.

Reach Out and Read -Longwood Area

Read to young children(6mon- 4yrs), model book-sharing

atggacttacggcatgatctgttgacggcgatccagtttgaccagtgaccagtttttagggcaaatatatacgacagattcagcatgacttacggcatgacttacgacttacatgatctgttgacggcgatccagtttgaccagtgaccagtttttagggcaaatatatacgacatgacttacggcatgacttacgacttacgta

techniques for parents and show them by example that reading aloud is fun for parent and child.

Project Bread-The Walk For Hunger- North End

Work to advocate freedom from hunger across the Commonwealth. A main project is the walk for hunger.

The Boston Rescue Mission- Downtown Boston

Work in residential programs, with clients going through alcohol- and drug-recovery, or in their nightly shelter for homeless men.

GREATER Boston Food Bank- South Boston/Roxbury

Sort, categorize and distribute donated products to the hungry.

Boston Area Rape Crisis Center (BARCC)-Cambridge

Work in many areas dealing with rape awareness and rape survivors including the crisis hotline, the medical advocacy program, and legal advocacy.

Springwell, Inc.- West Boston

Work to keep individuals over sixty in their own homes safely and independently for as long as possible.

Casa Myrna Vazquez- Boston

Work with an organization that provides comprehensive services to women and children who are victims of domestic violence.

For more information on the above organizations including contact information and websites please visit the BBS Bulletin website at <http://www.hms.harvard.edu/dms/bbs/bulletin/index.html> and click on the link to the full community services article.

Faculty Profile: David Rudner

Assistant Professor of Microbiology and Molecular Genetics

Yao Chen (G3)

Research Interest:

Understanding basic mechanisms in bacterial differentiation, including cell-cell signaling and determinants of sub-cellular protein localization, with a budding interest in chromosome architecture and dynamics.

Beginnings: Rudner grew up in New York City. His mother is a microbiologist who, like Rudner, works on *Bacillus subtilis*. As a child, his mother often took him to the laboratory. To keep Rudner out of trouble, she would have him count colonies on bacterial plates. That is where the seeds were planted. Rudner majored in physics as an undergraduate at Oberlin College. However, he ultimately decided to work in biology, partly because it was difficult to be both a theorist and an experimentalist in physics. Biology offered him the opportunity to generate



hypotheses and do the experiments necessary to test them. Rudner's love for solving puzzles led him to Alan Grossman's laboratory at MIT. The two years he spent there had a tremendous impact on Rudner's intellectual growth. He decided to go to graduate school to study biology, and he fell in love with microbiology.

Graduate School and Beyond: As a graduate student at Berkeley, Rudner studied alternative splicing and sex determination pathways in *Drosophila*. He worked simultaneously on both the genetics (in Thomas Cline's lab) and the biochemistry (in Donald Rio's lab) of the splicing pathways specified by *Sex-lethal*, the master regulator that controls sexual dimorphism and dosage compensation. Through his studies, he learned an invaluable lesson in experimental research: what we learn in the test tube is not always true inside the organism. Therefore, it is a tremendous advantage to work in a system, such as *B. subtilis*, where one can easily do both. After graduate school, Rudner returned

Continued on bottom of facing page...

Recent BBS Student Publications

Asthana S, King OD, Gibbons FD, Roth FP. (2004). Predicting protein complex membership using probabilistic network reliability. *Genome Research* 14(6):1170-1175.

Beck LH Jr (recent grad), **Goodwin AM** (recent grad), D'Amore PA. (2004). Culture of large vessel endothelial cells on floating collagen gels promotes a phenotype characteristic of endothelium in vivo. *Differentiation* 72(4):162-7

Cohen HY, Miller C, **Bitterman KJ** (G5), Wall NR, Hekking B, Kessler B, Howitz KT, Gorospe M, De Cabo R, Sinclair DA. (2004). Calorie Restriction Promotes Mammalian Cell Survival by Inducing the SIRT1 Deacetylase. *Science* 305: 390-392.

Everley PA (G4), Krijgsveld J, Zetter BR, Gygi SP. (2004). Quantitative cancer proteomics: stable isotope labeling with amino acids in cell culture (SILAC) as a tool for prostate cancer research. *Mol Cell Proteo* 3:729-735.

Fukuto HS (recent grad), Ferkey DM, Apicella AJ, Lans H, Sharmeen T, Chen W, Lefkowitz RJ, Jansen G, Schafer WR, and Hart AC. (2004). G Protein-Coupled Receptor Kinase Function Is Essential for Chemosensation in *C. elegans*. *Neuron* 42: 581-593.

Chen J, Wall NR, **Kocher K** (G3), Duclos N, Fabbro D, Nueberg D, Griffin JD, Shi Y, Gilliland DG. (2004). Stable expression of small interfering RNA sensitizes TEL-PDGFBetaR to inhibition with imatinib or rapamycin. *J Clin Invest.* 113(12):1784-91.

Paez JG*, Janne PA*, **Lee JC*** (G5), Tracy S, Greulich H, Gabriel S, Herman P, Kaye FJ, Lindeman N, Boggon TJ, Naoki K, Sasaki H, Fujii Y, Eck MJ, Sellers WR, Johnson BE, Meyerson M. (2004). EGFR mutations in lung cancer: correlation with clinical response to gefitinib therapy. *Science* 304(5676):1497-500.

Lilley BN (G6) and Ploegh HL. (2004). A membrane protein required for dislocation of misfolded proteins from the ER. *Nature* 429:834-40

Lenz DH, Mok KC, **Lilley BN** (G6), Kulkarni RV, Wingreen NS, Bassler BL. (2004). The Small RNA Chaperone Hfq and Multiple Small RNAs Control Quorum Sensing in *Vibrio harveyi* and *Vibrio cholerae*. *Cell* 118:69-82.

McKee AE (G4), Silver PA. (2004). REF-ereeing the cytoplasmic fate of mRNA via nuclear export. *Dev Cell* 6(6):740-2.

Scherz PJ (G4), Harfe BD, McMahon AP, Tabin CJ. (2004). The limb bud Shh-Fgf feedback loop is terminated by expansion of former ZPA cells. *Science* 305(5682):396-9.

Han J-DJ, Bertin N, Hao T, Goldberg DS, Berriz GF, **Zhang LV** (G4), Dupuy D, Walhout AJM, Cusick ME, Roth FP, and Vidal M. (2004). Evidence for dynamically organized modularity in the yeast protein-protein interaction network. *Nature* 430(6995):88-93

*These authors contributed equally to this publication.

Announcements

Christopher Brown (G3) was recently engaged to Stephanie Thurston, a recent Cornell University graduate who is currently serving as an officer in the US Navy.

Christin Cvetic (G6) was engaged to Jarrett Munkittrick on July 17th in Philadelphia. An October 2006 wedding is planned.

Jason Heindl (G3) married Karen Wiesenauer on June 5th, in Ann Arbor, MI.

Kerry Kocher (G3) and Dan Brown were married on June 5, 2004 in Allentown, PA.

Congratulations to Elyan and **Abraham Rosenbaum** (G2) on the birth of a daughter, Maily, on July 14th.

to the East Coast to study *B. subtilis* sporulation in Richard Losick's laboratory at Harvard. He chose this topic because the field was open and a single lab could work on many interesting problems.

Hobbies: Rudner enjoys hiking and bicycling. He also has a passion for traveling, and strives to do so at every opportunity. Between his work at MIT and graduate studies at Berkeley, he traveled to Western Europe, Scandinavia, and Eastern Europe. After graduate school, he spent three months

wandering through Hungary, Romania, Bulgaria, Turkey, Syria, Jordan, and Israel. Prior to starting his lab at Harvard Medical School, he spent time in France and the Netherlands. He loves the anthropological aspect of his travels, and is especially interested in countries that don't have a strong Western influence. He enjoys the experience of seeing and feeling a place and time that are unfamiliar.

Faculty Profile: David Fisher

Department of BCMP & Associate Professor of Pediatrics

Maria Naylor (G2)

Research Interests: The Fisher lab seeks to understand the roles of helix-loop-helix transcriptional regulators, such as MITF, in development and cancer. In addition to utilizing basic biochemistry, cell biology, and animal models, the lab adopts a clinical perspective to approaching basic science questions, and is involved in clinical trials for melanoma and other diseases.

Beginnings: Fisher grew up in New Jersey and was exposed to experimental science from an early age by his father, a biochemistry professor at Rutgers. Despite some entertaining and expensive laboratory mishaps (including one that destroyed thousands of dollars worth of chromatography equipment in his father's lab), Fisher loved science and majored in biology and chemistry at Swarthmore College. A defining moment in Fisher's scientific career came when he was a summer student in Bob Weinberg's lab. He was given a project to transfect 3T3 cells with various samples of cancer DNA, in order to determine if real cancers contained genes capable of producing transformed foci. One of his samples succeeded and was eventually traced to a new oncogene: Ras.

Graduate School and Beyond: Fisher earned his M.D./Ph.D. at Rockefeller University and Cornell Medical College,



working on a joint project between the labs of Henry Kunkel and Günter Blobel that involved snRNP biosynthesis and its roles in auto-immune diseases. His post-doctorate work in Phil Sharp's lab at MIT focused on Myc DNA recognition and binding. Recruited to Harvard in 1993, Fisher heads the melanoma

program at Dana-Farber and also treats cancer patients at Children's Hospital.

Odds and Ends: The profession of his mother, a musician, greatly influenced Fisher as well. As an undergraduate at Swarthmore, he also studied cello at the Curtis Institute of Music. He later won the Artists International Competition and performed at Carnegie Hall. Above all, he admires his father for successfully balancing work and family, and aspires to do the same himself. Although Fisher no longer plays the cello quite as extensively, his time is filled by running his lab and participating in activities with his four sons.



Goldenson Building , Room 129
Harvard Medical School
220 Longwood Avenue
Boston, MA 02115