MCB Transcript

Fall 2004 • Vol. 7, No. 2

Newsletter for Members and Alumni of the Department of Molecular & Cell Biology at the University of California, Berkeley

Berkeley Eyes Stem Cell Research

California voters have approved a bond measure that is likely to make the state a world center of human embryonic stem cell research. Now a number of Berkeley scientists, including many in MCB, are preparing to compete for a share of the bond proceeds in order to establish a leading role for Cal in this rapidly growing field.

Proposition 71, which passed by an 18 point margin on November 2nd, will provide $3 billion over ten years for human embryonic stem (ES) cell research in California. The measure was intended to close a funding gap left by the current Bush administration policy, which bars the use of human ES cell lines made after August 2001 in federally funded projects.

Human ES cell research is likely to advance biomedicine in several ways. For stance, scientists would like to study the cellular defects that spark certain degenerative diseases such as multiple sclerosis and Lou Gherig's disease, but most of these defects have already occurred by the time symptoms arise. With ES cells derived from embryo clones, researchers may be able to recapitulate the presymptomatic stages of a disease in a dish. Another widely anticipated outcome of ES cell work is the development of cell-based therapies to replace ailing cells in the body.

Proposition 71 has created something like a mini-National Institutes of Health (NIH) in California. The new Institute for

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Chancellor Birgeneau accepting his nomination by Lt. Gov. Cruz Bustamante (center) to help oversee Prop. 71. BMB professor Randy Schekman looks on. Photo credit: Steve McConnell

Model Diversity Program Wins Large Grant

BSP Graduate Ramon Pineda tutors current members

A unique Berkeley program that gives students from underserved communities a boost towards careers in science and medicine has received a $5.6 million grant to further its goals. The money will both enhance the program for current students and put it on track to become a national model for efforts to level the playing field for students of all backgrounds who are interested in the biological sciences.

Co-founded in 1992 by Berkeley academic support specialist John Matsui, MCB professor Caroline Kane (BMB) and former professor Corey Goodman (Neuro), the Biology Scholars Program has already helped launch the careers of hundreds of students, mostly from minority groups, whose backgrounds might not have fully prepared them to excel at college-level work.

"The minority students in the program graduate in biology at the same rate

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. . . *Model Diversity Program continued from page 1*

and with the same grade point averages as non-minority students," says Matsui, who has directed the program since its inception. "That's unheard of, since they come less well prepared," he adds. Minority students typically enter Berkeley with lower SAT scores and grade point averages. "We have closed the majority-minority gap," says Matsui.

The Biology Scholars Program (BSP) is not for minority students only, but rather is open to all students with an interest in biology who have a demonstrated commitment to serving the underserved. Priority is given to students from low-income families or who are the first in their families to go to college. Next in line are students who have participated in academic development programs such as Summer Bridge, which prepares newly-admitted freshmen to enter Cal.

In this way, BSP avoids the pitfall of improving diversity merely by skimming the most academically well-prepared from the available pool of freshmen. By looking for signs of potential beyond grades, it expands participation of people from underserved communities in the sciences. "This is what the science community must do to enlarge and diversify the pool of those who succeed in science majors and careers," says Matsui.

Until now, the program was funded entirely by the Howard Hughes Medical Institute. The new grant, announced on November 9, comes from the San Francisco-based Gordon and Betty Moore Foundation, which funds high-impact projects in science, environmental conservation and higher education. "This generous grant is going to pay dividends not only for our students, but also for the well being of the communities they will serve when they complete their studies," said Berkeley Chancellor Robert Birgeneau in a press release.

Assistant Director Roger Liu, Director John Matsui, and Program Assistant Marco Angulo.

The bulk of the new grant will go towards enhancing BSP services for students already in the program. "We will be keeping the same number of students, but improving the quality of the experience," says BSP Assistant Director Roger Liu. The program currently has 450 students enrolled. Although the program is administered by MCB, students may select from a variety of biology and healthcare-related majors. Each student has access to individual mentoring, an academic and career seminar series, paid research internships both on and off campus, social events, career counseling, academic tutoring and study groups.

The new money will bring additional mentoring and academic resources to all BSP students. In addition, BSP will now provide a variety of career 'pathways' in biological research and the health sciences. Pathways are individualized combinations of mentoring, internships and research experience that help students achieve a particular career goal. For example, in Spring 2005, a newly developed medical pathway will provide 60 pre-med students each year with medical mentoring by physicians, paid internships and financial assistance to attend conferences and to pay for medical school applications and review courses.

"It's really a guiding and supportive environment," says BSP graduate Youssra Marjoua. BSP mentors don't just help you academically, they look at emotional, social and familial factors, because they know that is often what drives academic success," she says.

Youssra Marjoua

Marjoua was an MCB major who graduated in May. She is now tutoring current BSP students and working for a non-profit center within the School of Public Health while she prepares her medical school applications. When she came to Berkeley, she knew she wanted to be involved in public health, but it was the opportunities and guidance she found at BSP that helped her realize she wanted to be a physician. "It renewed my confidence," she says. "I no longer feel pursuing medicine is a big hurdle, but a gradual process I can enjoy along the way."

A critical component of the Moore Foundation grant is the $1 million specifically allotted to sharing the BSP approach with other California colleges and universities. The aim is to foster the creation of at least 10 similar programs elsewhere. If Matsui has his way, it won't stop there. "Our intention is to make this a national model," he says.

MCB Transcript

The MCB Transcript is published twice a year by the Department of Molecular and Cell Biology at the University of California, Berkeley.

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Current and past issues of the newsletter are available on the MCB web site (http://mcb.berkeley.edu/news).

. . . Stem Cell Bond continued from page 1

Regenerative Medicine will set priorities, fund projects, build buildings and write guidelines for ES cell research in the state. Prop. 71 has also amended the state constitution to guarantee a right to do human ES cell work and authorized a bond issue of around $300 million per year to pay for it all.

As Chair of the Chancellor's Advisory Committee on Biology, BMB professor Randy Schekman has the task of coordinating Berkeley's bid for Prop. 71 grants. On 15 November, he helped Lieutenant Governor Cruz Bustamante announce the nomination of Berkeley Chancellor Robert Birgeneau to the Independent Citizen's Oversight Committee, the 29-member body that will manage the new institute.

Interest in doing Prop. 71 research at Berkeley is high. At least 25 researchers from various departments have said they would like to participate in the first round of applications. Among them are MCB professors Richard Harland (G&D), John Ngai (Neuro), Mu-Ming Poo (Neuro), David Raulet (Immuno), Ellen Robey (Immuno), Mark Schlissel (Immuno), Robert Tjian (BMB), and Astar Winoto (Immuno). And even though he works mainly with yeast, Schekman says he is also considering the possibility of using human ES cells in his own lab to study protein traffic issues involved in diseases like Alzheimer's.

The types of projects Berkeley researchers are likely to propose can be slotted into two categories. One involves basic questions about cell differentiation, such as how external cues send cells down specific developmental pathways. "We have a really strong developmental biology group here, and that is the key to unlocking the potential of stem cells," says Tjian. The other group involves researchers like Kevin Healy in the Bioengineering Department who would like to develop ways of organizing stem cells into tissues suitable for transplantation.

The potential new source of research dollars is welcome relief after four years of state cutbacks have forced MCB and other departments to trim their costs (see budget update, page 5). Still, even if Berkeley wins several grants under the proposition, it will do very little to close the gap, Schekman says. "No way this money makes up for the big cuts we have suffered," he says. "I don't see Prop. 71 adding significantly to the MCB Department budget."

But it's not just the money that has researchers excited. Since 2001, there has been growing concern over the usefulness of the roughly 20 human ES cell lines now available from the NIH. All of them are grown on mouse 'feeder' cells, which supply essential nutrients, but which could complicate experiments. And many of them do not grow very well. The problem is that too little was known about how to derive ES cell lines back when those lines were made, Tjian says. "With Prop. 71 we can immediately go for better cells and drop the current ones," he says. "I'm not sure you want to do many experiments on established lines until you know how to establish them better."

Preparations have begun for Berkeley to become involved in making new human ES cell lines. The university is seeking a source of early-stage embryos, or blastocysts, to supply the undifferentiated tissue from which the cells are taken. These would most likely come from a fertility clinic which has excess frozen embryos from fertilization procedures as well as consent from the donors to use them in research. Consideration is also being given to the need for separate lab space in which to carry out the work, so that federal guidelines barring the use of new lines in NIH-funded labs are not violated.

How Berkeley will fare in the competition for Prop. 71 grants remains to be seen. As the *Transcript* went to press, the oversight committee charged with managing California's new Institute for Regenerative Medicine was still being nominated. Once complete, that committee must nominate 15 researchers— who are not themselves vying for any of the funds—to review grant applications. It must also put out program announcements detailing the types of grants to be awarded and setting application deadlines. All that could take well into the new year.

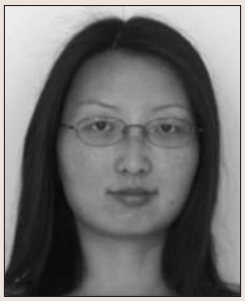
But Tjian is optimistic. The lack of a medical school at Berkeley doesn't really matter, he says, since clinical trials of any potential stem cell therapies are years away. What is important now is a strong grounding in basic research based on model organisms from which insights into the workings of human cells can be gleaned. "You can't build a program of any depth without it, and that's where we have a huge edge," he says.

Bioengineering professor Kevin Healy (center) describes tissue culture methods to Lt. Gov. Cruz Bustamante in front of reports. Photo credit: Steve McConnell

FACULTY NEWS

Sharon Amacher (G&D) and **Laurent Coscoy** (Immuno) have each received a UC Berkeley Hellman Family Faculty Fund Award for 2004-2005. The grant is intended to support outstanding young faculty members after their start-up funds are exhausted and before they have had time to develop sufficient extramural sources.

Richard Calendar and **Dan Portnoy** (BMB) are participating with Cerus Corporation in a joint grant from the National Institute of Allergy and Infectious Diseases to make a better anthrax vaccine. They use UV light to kill a strain of *Bacillus anthracis* that is susceptible to DNA cross-linking, a method which should produce a highly immunogenic vaccine. They are developing other genetic tricks to further enhance its potency.



▲ **Lu Chen** (Neuro) is one of 16 winners of the 2004 Packard Fellowships in Science and Engineering, given by the David and Lucile Packard Foundation. Each Fellow receives an unrestricted research grant of $625,000 over five years.

Michael Eisen (G&D) was honored—along with 4 other Berkeley junior faculty—with the 2003 Presidential Early Career Award for Scientists and Engineers in a ceremony at the White House on September 9, 2004. The award is the nation's top honor for scientists in the early stages of their careers. Previous recipients of the award include MCB Professor in Residence Abby Dernburg in 2002 and Professor Carolyn Bertozzi in 1999.

Gary Firestone (CDB) received the 2004 Rhoda H. Goldman Award for Distinguished Faculty Advising of Undergraduates.

John Forte (CDB) traveled to the United Arab Emirates in December to receive the Hamdan Award For Medical Research Excellence for his work in gastrointestinal physiology and cell biology. Forte's lab has worked out how the stomach makes its acid. Their identification of the specific acid pump enzyme, called the H,K-ATPase, led to the development of widely used anti-secretory drugs including Prilosec, Nexium, Protonix, and Aciphex.

Richard Harland's (G&D) lab is featured in a *Nature* Milestones article, (available online at http://www.nature.com/milestones/development/milestones/full/milestone19.html) which describes their seminal work in elucidating the molecular basis of neural induction in the frog.

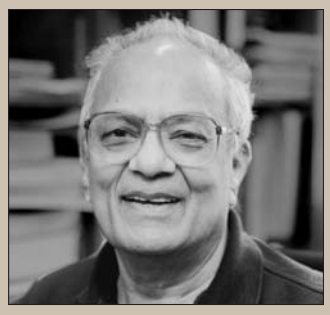
Nicole King (G&D) has received the George A. Bartholomew Award from the Society for Integrative and Comparative Biology (http://www.sicb.org/). The annual prize is given to a young investigator for distinguished contributions to comparative physiology and biochemistry or to related fields of functional and integrative biology.

▲ **Jack Kirsch** (BMB) gave a plenary lecture at Reaction Mechanisms VII in July in Dublin, Ireland.

Michael Marletta (BMB) was awarded the Harrison Howe Award by the Rochester Section of the American Chemical Society. The award is granted for outstanding contributions to research in chemistry and consists of a plaque and an honorarium. Of the 61 previous Howe recipients, 24 have gone on to win the Nobel Prize.

Daniel Portnoy (BMB) has received a Senior Scholar Award in Global Infectious Disease from the Ellison Medical Foundation. The awards emphasize projects less likely to be supported by traditional sources because of their perceived novelty or high risk, or because the investigator is moving into a new research area. Scholars receive up to $150,000 per year for a four years. Portnoy is studying the host response to *Listeria* and tuberculosis infections.

Jeremy Thorner (BMB) has won the 2004 Award for Distinguished Research Mentoring of Undergraduates in the Biological Sciences given by the College of Letters and Science. He also participated in the site visit committee for the Quinquennial Review of Cancer Research at the Biomedical Research Centre of Ninewells Hospital in Dundee, Scotland.



Breast cancer researcher **Satyabrata Nandi** (CDB) has retired and assumed status as Professor Emeritus. Nandi received his Ph.D. in zoology from UC Berkeley in 1958 and has been here ever since, initially as an assistant research endocrinologist. He was hired as an assistant professor in 1962 and made full professor in 1968. He was chair of the Dept. of Zoology from 1971-1973 and Director of the Cancer Research Laboratory from 1974-1984.

UC Budget Update

The final budget approved by the state legislature in August included a 6% cut in funds for the University of California system. But it could have been worse. Governor Arnold Schwarzenegger had originally proposed to cut UC freshman enrollments by 10%, but the final budget eliminated that reduction. UC outreach programs for K-12 academic development were also preserved.

For MCB, the cuts translated into a 2.25% permanent funding reduction ($280,391) and a 3.75% temporary reduction of $456,805. Geoffrey Owen, Dean of Biological Sciences and Professor of Neurobiology, has agreed to cover the entire temporary reduction for this academic year (2004-2005) from his office's discretionary funds. The permanent reductions are covered by staff positions in MCB that were intentionally left vacant when staff retired to help the department weather the budget storm (see Spring 2004 *Transcript*).

The state budget situation for next year is still unknown, but UC President Robert Dynes suspects the worst is over. "This is the fourth year of cuts for the University of California, but it appears we are at last turning a corner," he said in a 2 August press release.

Stanley Hall Replacement Continues Apace

The steel skeleton of the molecular engineering building, which replaces Stanley Hall at the top of campus, has risen from the 3-story-deep hole dug late last year. The new building should be ready for occupation in the first half of 2006.

2003–2004 GRADUATES

FALL 2003

- **Eric Abbate** (Botchan) Crystal Structure and Biochemical Analysis of an E1:E2 Complex of the Human Papillomavirus Type 18
- **Zev Bryant** (Bustamante) Single-Molecule Mechanics of DNA and Associated Enzymes
- **Jeremy Burt** (Chamberlin) In Vitro Characterization of the Transcript Cleavage Reaction of *E. Coli* RNA Polymerase
- **Ciro Cecconi** (Bustamante) Studies of the Mechanical Unfolding and Refolding of RNase H and T4 Lysozyme
- **Danica Chen** (Zhou) HIV-1 Tat Targets Microtubles and a Microtubule-associated Death Molecule Bim to Induce Apoptosis
- **Michelle Chernock** (Winer) Connections and Neurochemistry of the Rat Inferior Colliculus
- **L. Noel Clark** (Isacoff) Reconstructing K+ Channel Domain Rearrangements from Dozens of Local Nanospace Measures of Gating Motion
- **Camin Dean** (Isacoff) Function of Neuroligin and Neurexin During Synapse Formation in the Central Nervous System
- **Mehagan Hopkins** (Handel) (MA)
- **Elizabet Kitchens** (Robey) The Role of Numb in T-cell Development and Signaling
- **Cary Lai** (Collins) Roles and Mechanism of the Telomerase Catalytic Components
- **Jessica Palmer** (Goodman) Genetic Analysis of Signaling Pathways Involved in *Drosophila* Embryonic Axon Guidance
- **Erik Pierstorff** (Kane) In vivo and in vitro Characterization of *S. cerevisiae* CTD Phosphatase, Fcp1
- **Susan Schwab** (Shastri) Cryptic Translation of Antigenic Peptides
- **Kris Srinivasan** (Calendar) Testing Site-specific Plasmid Integration In *Schizosaccharomyces pombe* Using the Recombinase and Attachment Sites from Phage U153 (MA)
- **Michael Stone** (Cozzarelli) Single Molecule Studies of DNA Twisting and the Mechanism of Type II Topoisomerases
- **Tammy Wu** (Meyer) A Sex-specific Lethal Mutation Identifies NOX-1, a Component of a *C. elegans* Protein Complex Implicated in Histone Modification

SPRING 2004

- **Sara Agee** (Weisblat) Developmental Significance of a Maternally Expressed *nanos* Homolog, *Hro-nos*, in the Leech *Helobdella robusta*
- **Theresa Allyn** (Thorner) (MA)
- **Daniel Baggott** (Schekman) (MA)
- **Audrey Duarte** (Knight) The Effects of Aging and Prefrontal Cortical Damage on the Neural Correlates of Recollection and Familiarity
- **Rachel Fennell-Fezzie** (Berger) Structural and Functional Studies of *Escherichia coli* Condensin
- **Alexa Franco** (Kaufman) Co-regulation of Chromatin Assembly and DNA Replication
- **Robert Froemke** (Dan) Long-term Synaptic Plasticity in the Visual Cortex
- **Ramona Gonzales** (Portnoy) A Cytosol-specific Gene Expression Program Induced by Gram-positive Intracytosolic Bacteria
- **Giovanna Guerrero** (Isacoff) Heterogeneous Transmission at the *Drosophila* Larval Neuromuscular Junction Revealed by Single-Bouton Optical Imaging
- **Christin Hardy** (Cozzarelli) Control of Chromosome Topology in *Escherichia coli*
- **Elaine Lau** (Handel) Regulation of Chemokine Function by Glycosaminoglycan Binding and Oligomerization
- **Edwin Lee** (Flannery) Transport of Outer Segment Proteins in Animal Models of Retinal Degenerations: Disease Mechanisms and Potential Therapies
- **Erik Miller** (Marqusee) Topology and Stability in Protein Folding Pathways
- **Hanspeter Niederstrasser** (Nogales) XMCAK Is a Kinesin with Depolymerization Activity Mediated by Unique Microtuble Interacting Domains
- **Martin Powers** (Thorner) (MA)
- **James Priest** (Rubin) (MA)
- **Elizabeth Shank** (Marqusee) An Investigation of the Single Molecule Behavior of RNase H
- **Kathleen Stauber** (Firestone)
- **Moriah Szpara** (Ngai) Factors Affecting the Outgrowth and Guidance of Neurons during Development
- **Hera Vlamakis** (Zusman) The Regulation of Type IV Pilus Mediated Motility by Multiple Chemotaxis Pathways in *Myxococcus xanthus*
- **Tyler Alioto** (Ngai) Molecular Diversity of Odorant Receptors in Zebrafish
- **Keren Witkin** (Collins) Affinity Purification of a Telomerase Holoenzyme from *Tetrahymena thermophila*

CLASS NOTES

- After graduation**, Suren Ambegaokar** (BA 2003) worked as a research associate in Greg Cole's lab at UCLA, where he studied the cellular and molecular processes involved in Alzheimer's disease as well as possible therapeutics. Ambegaokar then began the Ph.D. program in neuroscience at UCLA this Fall, and plans to continue studying neurodegeneration and learning & memory. (surenambe@berkeley.edu)

- **Chien-Ju Alice Chen** (BA 2000) is a patent litigation attorney with Fenwick & West LLP, a Mountain View law firm. (roo@boalthall.berkeley.edu)

- **Matthew S. Falk** (BA 1994) is a resident physician in nuclear medicine at UCSF. He graduated from medical school at Yale in 2000 and did an internship at Stanford in 2001. His residency will be complete at the end of the academic year, after which he plans to continue with either a fellowship or associate position. Falk is also engaged to be married in the summer. (matthew_falk@aya.yale.edu)

- **Andrew H. Guo** (BA 1995) is an MD and a fellow in occupational medicine at Loma Linda University since 2000. He is pursuing an executive MBA at the University of Southern California's Marshall School of Business, and plans to look for opportunities in medical management after his fellowship is complete. Guo says he remains a dedicated Cal fan. (andrew.guo.2006@ marshall.usc.edu)

- **Jennifer Lee** (BA 1999) is living and working in Micronesia as a Supreme Court attorney in the Mariana Islands. She is also a freelance writer and she travels extensively in the South Pacific, Asia, and Down Under. (jlee@justice.gov.mp)

- **David Nierengarten** (PhD 2003) works at Research Corporation Technologies, a venture capital fund that invests in early stage biotechnology and medical device companies. He says if you want to drop him a line about your great idea, please go ahead. (dnierengarten@rctech.com)

- **Meenakshi Palani** (BA 2003) took a year off of school to work as an ayurvedic lifestyle consultant and to set up clinics around the country with an ayurvedic doctor from India. Palani started medical school this semester at Des Moines University in Iowa to work toward a degree in osteopathic medicine.

- **Graham Scanlon** (BA 2000) is a third year medical student at UC San Diego School of Medicine. He received Honors in Pharmacology, Histology, Psychopathology, and Introduction to Clinical Medicine (physical exam skills course). He conducted pain research in 2003 which led to two presentations at national conferences and a paper now in review. (gscanlon@ucsd.edu)

- **Isaac Yang** (BA 2000) has been a general surgery intern at UCSF since June.

CLASS NOTES WANTS TO HEAR FROM YOU

Do you have a Bachelor's, Master's or PhD in Molecular and Cell Biology from Berkeley? Let your classmates know what you are up to by sending in a Class Note for publication in the next issue.

To send your Class Note, you can

➜ Clip and mail this form
or
➜ go to mcb.berkeley.edu/alumni/survey.html
or
➜ Send e-mail to tscript@berkeley.edu

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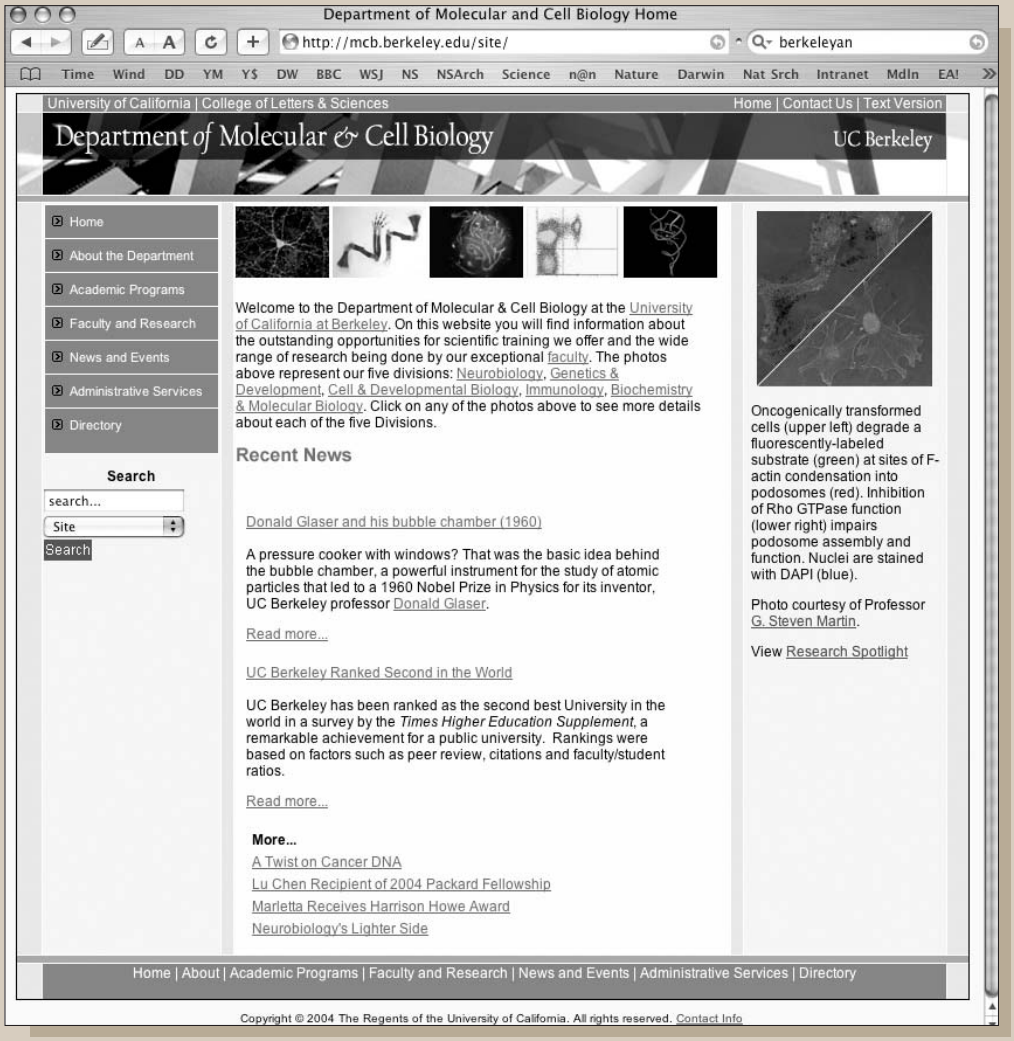
Introducing MCB's New Website

Surf over to mcb.berkeley.edu and check out the Molecular and Cell Biology Department's new home page. Not only is the redesigned site more attractive and easier to navigate, it also features frequent news updates and a regular Research Spotlight, highlighting department research through colorful images from various labs. Here you can also read past issues of the *Transcript* and submit your Class Note for publication in a future issue. Much credit for the redesign goes to Karin Hansen, MCB's web guru with help from the campus multimedia services group.



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