Fall Semester saw a raft of appointments and promotions in MCB. Richard Harland took over for Geoff Owen as department chair, Mark Schlissel became vice chair, and Robert Tjian took the title of Faculty Director of the Health Sciences Initiative (see p. 3 for details). With all this shuffling at the top, the real news was easy to overlook. In August, the department established an entirely new entity: the MCB Development Committee.

In fact, the new committee signals a sea change in the way MCB goes about financing its operations. This year, one of the department’s funding mainstays, a large training grant from the National Institutes of Health, was slightly reduced, and a generous annual contribution from the Howard Hughes Medical Institute in support of graduate education came to an end. This unfortunate confluence of events has led the department to seek additional funding. The job of the Development Committee, headed by Biochemistry and Molecular Biology Professor Jeremy Thorner, is to seek out new opportunities for fundraising wherever they may lie. It now appears that the future holds a much greater reliance on industry sponsorships, endowed chairs, and good old philanthropy.

On the one hand, costs are rising. To ensure that Berkeley remains at the forefront of biological research, the department is now in the midst of an extremely successful drive to recruit new and energetic young faculty. The result has been three to four new faculty per year, mostly new assistant professors still in the midst of applying for their first grants as principal investigators. Some of the rising stars that MCB has recently hired include Rebecca Heald, James Berger, Matthew Welch, Eva Nogales, Sharon Amacher, Karsten Weis, Richard Kramer, David Bilder and Jamie Cate to name a few (see previous newsletters for profiles). All received help from the department to cover costs such as lab renovations, new equipment purchases and technician salaries, as well as money from the training grant to pay graduate student stipends. The trend continues. Three of the four new faculty profiled on page 4 of this newsletter are starting new labs. And of course the recruitment of established faculty, such as recently hired structural biologists John Kuriyan and Jennifer Doudna, comes with its own cost of relocating an operational laboratory and its members.

Add to this the rising cost of doing cutting-edge science, and it becomes clear that the department is in greater need of financial resources than ever before. The post-genomic era has redefined what is essential to doing biology. Gel boxes and centrifuges are no longer adequate. Now it takes microarray readers, confocal microscopes, mass spectrometers, and X-ray beamlines—just to name a few of the big ticket items that are expensive to acquire and operate but indispensable to the department’s research mission. For example, a new mass spectrometer typically costs several hundred thousand dollars.

continued on page 6 . . .
Rich Calendar (BMB) was elected to the Editorial Board of *The Journal of Bacteriology* and was made an editor of *Plasmid—A journal of microbial genomes and genome dynamics*.

Michael A. Marletta (BMB) was appointed the Aldo DeBenedictis Chair in Chemistry.

Kathleen Collins (BMB) will receive the fourth annual American Society for Cell Biology-Promega Award for Early Career Life Scientists at the ASCB Annual Meeting in San Francisco in December.

Richard Harland (G&D) was promoted to chair of the department on July 1 after the previous chair, Geoff Owen, was named dean of the Biological Sciences Division in the College of Letters & Science. Mark Schlissel was named vice-chair.

Caroline Kane (BMB) officially became a member of the National Advisory Council of the National Center for Minority Health and Health Disparities at the NIH.

Paul Kaufman (G&D) was promoted to career Staff Scientist at Lawrence Berkeley National Lab and Associate Adjunct Professor in MCB as of July 1.

Daniel Koshland Jr. (BMB) was the first recipient of the Westheimer Medal, established this year by Harvard University in honor of Frank Westheimer, Morris Loeb Professor of Chemistry Emeritus at Harvard and a pioneer in biological chemistry. Koshland was a postdoc at Harvard from 1949–51. The medal is given for outstanding achievement in organic or biological chemistry.

Steve Martin (CDB) was appointed Richard and Rhoda Goldman Professor of Biology.

Robert Mortimer (G&D, Emeritus) has received the 2002 George W. Beadle Award, given by the Genetics Society of America for distinguished service to the field of genetics and the community of geneticists. Mortimer shares the award with Andre Goffeau, a yeast geneticist at the Université Catholique de Louvain, Belgium, for their contributions to the development of yeast as a genetics system. Mortimer also established the Yeast Genetic Stock Center, which has been tremendously useful to the entire community of yeast geneticists.

Gunther Stent (Neurobiology, Emeritus) received the 2002 John Frederick Lewis Prize at the November meeting of the American Philosophical Society for having written the book-length philosophical essay “Paradoxes of Free Will”. The Lewis Prize is awarded to the author of the best book or monograph published by the Society in any given year.

Jeremy Thorner (BMB) was appointed to a four-year term as a Member of the Committee on Awards of the American Academy of Microbiology, the honorific arm of the American Society for Microbiology, on July 1. On the same date, he was also appointed a Member of the Editorial Board for the Molecule Pages of the Alliance for Cell Signaling, operated out of UT Southwestern Medical School in Dallas.


Robert Tjian (BMB) was appointed Faculty Director of the Berkeley Health Sciences Initiative, a campus wide health research collaboration. For more on the HSI, visit www.urel.berkeley.edu/health_sciences.
It has been a good year for Cell & Developmental Biology Professor Randy Schekman. In May, he was chosen to chair the Biochemistry section of the National Academy of Sciences. Then in July, he took the helm of the Jane Coffin Childs Memorial Fund for Medical Research, which awards competitive grants for post-doctoral research. In December, he received the Louisa Gross Horwitz Prize of Columbia University, given to recognize exceptional accomplishments in biological and biochemical research.

But perhaps best of all, he shared the Albert Lasker Award for Basic Medical Research with James Rothman of the Sloan-Kettering Institute in New York City. The Lasker Awards are considered to be one of the two top honors in science, and 66 Lasker Award recipients have gone on to win Nobel prizes.

In pioneering work begun in the 1970s, Schekman and Rothman independently elucidated the mechanisms by which proteins travel between cellular compartments. They worked out the first molecular details of vesicle transport, in which tiny membrane-bound packets of protein ferry their cargo by first budding off of one cellular compartment and then fusing with another. This intracellular trafficking, which can culminate in secretion from the cell, is critical to numerous biological phenomena, from the communication of nerve cells to the release of adrenaline. Many viruses co-opt the secretory system to escape one cell and infect others, and abnormalities in secretory pathways underlie various diseases such as diabetes and possibly Alzheimer's disease.

Schekman and Rothman attacked the problem of trafficking from two divergent angles. Rothman took a biochemical approach, attempting to reconstitute transport pathways in the test tube with membranes and proteins extracted from cells. Schekman chose the genetic route. As an Assistant Professor at Berkeley in the late 1970s, he began by isolating yeast mutants in which he could find vesicle traffic jams. In this way, Schekman and graduate student Peter Novick identified the first two secretory genes, sec1 and sec2, both of which turn out to be highly conserved and essential to secretion in organisms from yeast to humans.

Today, the once isolated niche of cellular transport has exploded to form a field in its own right, and in the process has influenced numerous other fields from neurobiology to embryology. Schekman and Rothman received their awards during a luncheon ceremony September 27 at the Pierre Hotel in New York City.
A corollary to Newton’s observation might be: to understand a complex and confusing thing, one should begin with its simplest components. Assistant Professor of Neurobiology Lu Chen is taking that approach to the synapse by attempting to build one from scratch.

Chen says her inspiration was a paper from former MCB Professor Tito Serafini’s group. Serafini demonstrated that non-neuronal cells could attract an axonal projection from a neuron if they expressed a particular neuronal protein. The projected axons appeared normal and were capable of forming synapse-like structures with the non-neuronal cells. So, Chen reasoned, it should be possible to complete the artificial synapse by engineering additional factors into the heterologous cells.

The first step to making the receiving terminal of the synapse is to incorporate neurotransmitter receptors. Chen has already found that when she co-expresses AMPA receptor subunits in human embryonic kidney (HEK) cells with two receptor-associated proteins, stargazin and PSD-95, the subunits cluster on the cell surface as they do in a normal postsynaptic cell. She next plans to add neuroligin, the molecule that stimulates presynaptic innervations and transmitter release. It turns out that neuroligin also binds to PSD-95, suggesting a possible functional interdependence.

In this way, Chen hopes to put a synapse together one piece at a time. While it is possible these four proteins might together simulate aspects of synaptic behavior, Chen suspects the story is more complicated. “We’re not sure whether the four components will work yet,” she says. “Probably something more will be needed.”

Besides contributing to a better understanding of the way neurons communicate, an artificial synapse would be a powerful tool for testing the function of new synaptic proteins as they are identified. There are many proteins, besides those essential for transmission, which regulate the synapse.

Chen spent much of Fall Semester moving from UCSF, where she was finishing a postdoc with Roger Nicoll, and setting up her lab in LSA. She will be able to take her first graduate students in January.

Viruses have evolved dozens of tricks to evade the defenses of their hosts. The herpesvirus that causes Kaposi’s sarcoma, one of the principle complications of AIDS, does it by preventing the cells it infects from alerting the immune system. As a postdoc in Donald Gannon’s lab at UCSF, Assistant Professor of Immunology Laurent Coscoy identified two of the proteins that Kaposi’s sarcoma-associated herpesvirus (KSHV) produces for this purpose. Dubbed MIR1 and MIR2, these virally-encoded transmembrane proteins cause the antigen-presenting immune complex MHC-1 to be tagged for destruction. Although MHC-1 reaches the cell surface normally in infected cells, it is then rapidly endocytosed before any immune response can be activated.

The main focus of Coscoy’s lab, which he set up in LSA in October, is to determine the molecular mechanisms by which MIR proteins target MHC-1, as well as two other cell surface proteins involved in immunity, B7.2, and ICAM-1. He is taking advantage of cell types in which MIR proteins have no effect on cell-surface molecules to screen for cellular factors that rescue the effect and that are therefore likely to be involved.

The mechanism of MIR protein action appears to involve ubiquitination of the target molecules. Coscoy has found eukaryotic homologs to MIR 1 and 2, suggesting there might be novel mechanisms of protein trafficking waiting to be discovered.

But MIR proteins are probably not the only mechanism of host defense avoidance that KSHV employs. Coscoy has noticed that MIR-expressing cells have an increased sensitivity to the immune cells known as natural killer cells, so KSHV must have some way of avoiding this effect. Coscoy’s group is now sifting through the 80-some genes of KSHV for other likely candidates in the virus’s game of cat-and-mouse. At the moment he has one rotation student. He will soon hire a technician and hopes to gain a postdoc in the near future.
Despite their much simpler molecular makeup, RNA enzymes, or “ribozymes”, have proven to be nearly as versatile as proteins in catalyzing chemical reactions. Researchers working on ribozymes have found them to be essential components of some of the cell’s most ancient and fundamental machinery.

One of the foremost scientists in the field today is Howard Hughes Medical Institute Investigator Jennifer Doudna, who moved her lab to Berkeley from Yale University at the beginning of the Fall Semester. Doudna began her career in the late 1980s as a graduate student and then postdoc for Jack Szostak at Harvard University. She published a series of ground-breaking papers on catalytic RNAs, including self-splicing introns and an RNA synthase.

Today, her lab is primarily engaged in three projects. One involves an RNA from hepatitis delta virus (HDV) that cleaves in different phases of the reaction.

A second project asks how certain viruses commandeer a cell's protein synthesis machinery. Many retroviruses, such as the hepatitis C virus (HCV), do this with a internal ribosome entry site (IRES), which recruits ribosomes more efficiently than cellular capped RNAs. Research scientist Hong Ji is now trying to understand this process with a combination of biochemical and X-ray crystallographic techniques.

Finally, postdoc Rich Spanggord is screening a library of small molecules for compounds that disrupt assembly of the signal recognition particle (SRP), a ribonucleoprotein complex attached to the beginning of growing proteins that are destined for secretion or entrenchment in the cell membrane. Such molecules could be used not only as tools to dissect the function of the SRP, but could also serve as the basis for cancer drugs or antibiotics.

Doudna joined the department two years ago as a Professor of Biochemistry and Molecular Biology, but continued temporarily at Yale on a leave of absence. Meanwhile, her four new postdocs borrowed space in the lab of her husband, Jamie Cate, who came to Berkeley in 2001. On November 3, Cate and Doudna celebrated the birth of their first child, a boy. Now the lab is in full swing with two second-year graduate students and two rotation students, as well as two technicians who came with Doudna from Yale.

What can a fruit fly in a glass of Chateauneuf-du-Pape tell about the wine? Does he recognize the characteristic spiciness of the southern Rhone? Can he spot the full fruit of a great year? In fact, remarkably little is known about how and what flies taste. They seem to have a penchant for beer, wine and rotten apples, but the neural circuitry that produces these behavioral preferences remains uncharted territory.

Kristin Scott has begun to make inroads. As a postdoc in Richard Axel’s lab at Columbia University, she characterized a large class of gustatory receptor genes (GRs), comprising some 60 members, in Drosophila melanogaster. Now as an Assistant Professor of Neurobiology in MCB, she has set out to trace the fly’s sense of taste from the moment a ligand binds to a receptor, to the activation of sensory regions of the fly’s brain, to the resulting behavior—feed, lay eggs, court female, for example.

Flies have taste receptor cells on their probosces, legs and wings. Only one GR gene is expressed in each cell, so each cell detects only one chemical compound, or ligand. This one-taste-per-cell feature gives Scott a powerful tool for determining what ligand each taste receptor is built to recognize. To do this, she links DNA encoding a cellular toxin to a given GR gene. All the taste cells that express that particular GR die. Scott then tests the fly on a battery of ligands to see which one it can no longer taste. These experiments are only just beginning, but she already has one promising candidate ligand for one of the GRs.

Scott’s main project at the moment is to map the regions of the fly’s brain that respond to different tastes. For this she has developed both functional and anatomical approaches. One approach involves flies engineered with a green fluorescent reporter that becomes activated when neurons are excited. The firing patterns that result from exposure to a specific ligand show up as glowing green neurons. Scott hopes to determine whether the fly brain groups receptors according to the ligand they detect, or whether they are organized according to where on the fly’s cuticle the receptor cell is located.

It’s exciting to be on the threshold of such a wide open area of research, Scott says. Not only is fly taste almost complete mystery, the receptor genes themselves are like no other known taste or smell receptors in the animal kingdom. “They look like they are from another planet,” she says. In fact, taste receptors in different types of animals rarely resemble each other. Taste appears to have evolved multiple times. Scott now has one graduate student and a technician who came with her from New York, but she hopes to grow quickly to a group of 6 or 7. Clearly there will be plenty for them to do.
Unfortunately, traditional funding sources have not kept up with the new needs. “We have been growing steadily, but we haven’t been growing as fast in terms of finances,” says Michael Botchan, head of the Biochemistry and Molecular Biology division. Worse than that, through an unfortunate coincidence, two key sources of funding were reduced this year.

One is the department’s largest training grant from the National Institutes of Health, which is also the largest awarded to any single department in the country. Until this year it covered the stipends of 55 graduate students at once for their first three years, relieving new faculty of the burden of paying graduate students so they can spend their limited research grant resources on supplies and equipment. But in the face of budgetary pressures, the NIH has reduced the grant to 50 slots.

Until this year, another critical source of money has been the Howard Hughes Medical Institute (HHMI). Previously, HHMI granted a lump sum to MCB every year for the department to spend on graduate student education. The amount was based on the number of graduate students in the labs of HHMI investigators. This was in addition to HHMI’s generous support of the labs themselves. But HHMI has phased out the lump payments in favor of more targeted funding to individual Hughes professors. This leaves the Graduate Affairs Office searching for a new wellspring to finance one of its most important activities: recruiting the best students to Berkeley.

Most professors agree, the department is only as good as its graduate students. So every year the MCB Graduate Admissions Committee selects between 150 and 170 of its 600-some applicants for on-campus interviews. This is a critical step in narrowing down the final class to around 50 students, both from the point of view of the applicants’ satisfaction with their choice of school and from the standpoint of the department, which seeks to recruit the cream of the crop. Previously, the cost of the many plane tickets and hotel rooms needed to pull this off was covered by Hughes money. But no more.

What to do? As head of the new Development Committee, Thorner is bursting with ideas. One is to establish several new endowed chairs in the names of senior faculty who have consulted for industry for many years. Endowing a chair is a way for the corporate beneficiaries of Berkeley’s expertise to recognize the value of strong relationships between academia and industry and to give something back to the research community.

Companies contacted so far have reacted positively, Thorner says, but no deals have yet been finalized.

Another approach is to revitalize the department’s Industrial Affiliates Program. This was first established in the early 1980s but was suspended a few years later as other funding became available. Companies that join the program commit a fixed amount each year. This could be anywhere from $10,000 to $200,000 depending on the agreement. In exchange, the companies get the chance to build relationships with faculty who may serve as consultants and with graduate students and postdocs in the department, who in turn may eventually seek employment in industry. Botchan, who led the program’s first incarnation, emphasizes that there are no strings attached to the money and there is no promise of intellectual property rights in return. “The companies have no influence over how the money is used,” Botchan says. “It just fosters good will both ways.”

Such programs have a proven track record at other institutions. Stanford University’s biosciences departments have had a very strong industrial relations program for years. Ted Tussing, Stanford’s development officer responsible for such deals, says some of the most effective arrangements are direct sponsorships of graduate students. Of course, the companies select laboratories doing work of interest to them, but the agreements are carefully crafted so that the students retain control over how they pursue their dissertation. The companies get reports on how the work is going, as well as access to the university’s talent pool. “It’s about talent not technology,” Tussing says. “The companies want to be close to where the action is.”

Thorner also hopes to appeal to the philanthropy of undergraduate and graduate alumni, former postdocs and those whose careers have benefited from their time in the department. On one end of the spectrum, he says, those whose entrepreneurial ventures have brought them significant rewards may wish to recognize the importance of MCB to their success. But he also hopes to find ways to reach out to all graduates who have gone on to fulfilling careers after their MCB training. In any case, it is now very easy for alumni to target their donations directly to MCB by going to Cal’s e-Giving website: givetocal.berkeley.edu. There is also a link under News and Events on the MCB web page at mcb.berkeley.edu.

Of course, new funds will benefit more than the department’s research program. More money in department coffers means better supplies for undergraduate laboratory classes, Thorner says. “Undergrads should do FPLC and not columns by gravity. They should set up crystal trays or do Affymetrix chips. Right now we can’t afford it.”

Thorner is confident the Development Committee’s efforts will meet with success. After all, Berkeley remains one of the jewels in the crown of biological research. It’s more than the success of its graduates or the impact of its research publications that draws top researchers to Berkeley, Thorner says. “There are only a handful of places around the world where there is that esprit de corps or elan that it takes to really get things done,” he says. “Berkeley is one of those places.”
### PANOS ASIMAKOPOULOS (BA 2001) 
Went to graduate school at the University of Patras in Greece to do a Master's degree in Medicinal Chemistry, a field that involves drug design and development. He started medical school at the University of Aberdeen in Scotland, UK this Fall. p_asimakopoulos@hotmail.com

### FRANCIS KA-MING CHAN (PhD 1996) 
Is an Assistant Professor in the Dept. of Pathology at the University of Massachusetts Medical School.

### SERENA HOM (BA 1999) 
After graduation, Horn spent a year studying at the UCSF School of Pharmacy, but then dropped out to pursue a career in investment banking. She is now a second-year investment banking analyst in Wachovia Securities Healthcare Group in Charlotte, North Carolina. She specializes in corporate finance and merger and acquisitions work in the life sciences sector. She is planning to join a private equity or venture capital firm before applying to business school. serena.hom@wachovia.com

### VICTOR LEE (BA 1993, Biochemistry and Psychology) 
After medical school at Tufts University, Lee completed a 3-year internal medicine residency at Kaiser Permanente in Los Angeles. He then worked as a hospitalist and has recently started a new career in healthcare information technology at Zynx Health in Beverly Hills. At Zynx, Lee develops clinical decision support modules for computerized physician order entry systems. viclee71@yahoo.com

### T. MICHAEL LIN (BA 1993) 
Finished his residency in dermatology at Thomas Jefferson University in June. He has moved back to California and now resides near Los Angeles. He and his wife Jennifer have a baby boy, David, who was born March. mlin2000@hotmail.com

### RACHITA SETHI (BA 2000) 
Worked for a year and a half as a consultant for ID Business Solutions, a software company in Emeryville, California, that targets the pharmaceutical and biotech industries. Sethi's software implementations helped companies get drugs on the market faster. In August, Sethi began a five-year MPH/MD program at St. George's University in Grenada, West Indies. Three of those years will be spent in the Caribbean and two in the US and the UK for rotations. rachita78@yahoo.com

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- Deepa Bhattacharya (Sha) NF-kB Mediated Regulation of Immunoglobulin Isotype Switching and Apoptosis.
- Peter Eimon (Harland) Characterization of members of the TGF-b superfamily and their antagonists in early Xenopus development.
- Åsa Engqvist-Goldstein (Drubin) The Huntingtin Interacting Protein 1 Related (Hip 1 R) Provides a Molecular Link Between the Actin Cytoskeleton and the Endocytic Machinery in Mammalian Cells.
- Peter Garber (Rine) Checkpoint Responses to Replication Defects in Saccharomyces cerevisiae.
- Thomas Harbaugh (Garriga) Cell Migration in Caenorhabditis elegans.
- Erica Kratz (Ngai) Elucidating the Transcriptional Regulation of Zebrafish Odorant Receptor Genes.
- Denise Krawitz (Kaufman) The Role of Chromatin Assembly Factor-1 in Heterochromatin Formation.
- Guochun Liao (Rubin) Bioinformatics Approaches in Drosophila P-Element Gene Disruption Project and cDNA Project.
- Lisa Megna (Cline) A Functional Analysis of Sex Determination in Drosophila viridis.
- Michael Miller (Collins) Molecules and Mechanism of the Tetrahymena thermophila Telomerase Ribonucleoprotein.
- Carrie Neff (Sachs) Genetic and Biochemical Studies on the Interaction Between Eukaryotic Initiation Factor (eIF) 4G and eIF4A from Saccharomyces cerevisiae.
- Pokala (Navin) Sivarama (Handel) Energy Functions for Protein Design.
- Shannon Stroschein (Luo) Regulation of Transforming Growth Factor- Signalining and the SnoN Oncoprotein.
- Chun Tsai (Meyers) Analysis of Caenorhabditis elegans genes with dual functions in dosage compensation and chromosome segregation.
- Fei Wang (Miller) Model for Choroidal Neovascularization (CNV) and Gene Therapy for Age-related Macular Degeneration (AMD).
- Joel Zupicich (Skarnes) Functional Analysis of Mouse Development Using a Gene Trap Approach and Genomic Analysis of Transmembrane Transcription Factors.

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- Andrew Finn (Kaplan) Mechanisms of Opiate Tolerance and Withdrawal Assessed by Gene Expression Analyses.
- Kael Fischer (Marqusee) Locating Autonomous Folding Units in Proteins.
- Rachel Fish (Kane) Biochemical and Genetic Investigations of Transcript Initiation and Elongation in Saccharomyces cerevisiae.
- Yick Fong (Zhou) P-TEFb and Associated RNPs in HIV Transcription and Coupled Pre-mRNA Splicing.
- Thomas Gerling (Lecar) Spatial Interactions in the Human Visual System Observed through Contrast Thresholds of Small Flickering Sources.
- Linda Liang (Sha) Regulation of B-cell Responses by the Transcription Factor, NF-kB and the Costimulatory Molecule, B7h.
- Botond Roska (Werblin) Vertical Interactions Among Parallel Image Representations in the Rabbit Retina.
- Giulietta Spudich (Marqusee) Interactions in the Folding Intermediate of Escherichia coli RNase H: Comparisons with the Native State Ensemble.