

MCB Transcript

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

Department Unveils

New Evo-Devo Center

The brave new world of genomics is upon us, but it's not quite what anyone expected it to be. Back when the era of big sequencing kicked off in the late 1980s, many people thought they would discover how different sets of genes produce different organisms. Now, with complete genome sequences piling up, biologists are facing a different sort of puzzle. "This is an extreme view," says Genetics and Development professor Michael Levine, "but the most surprising thing about the organisms sequenced so far is not how different they are but how much they have in common."

It turns out that what makes a fly a fly and a frog a frog may have less to do with their particular complements of genes than with the way those genes are expressed. Genome complexity does not appear to correlate with organismal complexity. Fruit flies have fewer genes than nematodes, for example. And the genes themselves are quite homologous. Roughly speaking, much of the animal life on Earth has redeployed the same basic set of genes in different ways to produce dramatically different results.

Berkeley is now poised to be at the forefront of the genomics research that will unravel these mysteries. With a grant of \$8.4 million from the Gordon and Betty Moore Foundation of San Francisco, MCB has launched the Center for Integrative Genomics (CIG) and has begun recruiting top researchers in bioinformatics and "evo-devo"—the interface between evolution and developmental biology. The



New Evo-Devo Star:
Parhyale hawaiiensis adult

principle labs will occupy space recently vacated on the 5th floor of LSA, but the center will also draw talent from other MCB labs, other departments, and the Joint Genome Institutes in Walnut Creek, where portions of the human genome and several other organisms were sequenced.

"Berkeley has a chance to combine bioinformatics, molecular biology and our current strengths in the development of model organisms to really build a program that is a bit different from what other major universities are doing," says Mike Botchan, head of the Biochemistry and Molecular Biology division.

One of the center's principle goals is to decode the regulatory DNA. When and where a gene comes on as an embryo develops can make a much bigger difference than a few changes to its amino acid sequence. There are many known examples. Vertebrate embryos sprout limbs wherever fibroblast growth factor (FGF) is expressed. Block FGF

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Visa Backlog a

Headache for Research

Getting a visa to study in the US has always been a hassle, but now people dream of the good old days. The immigration restrictions imposed after 9/11 are taking a serious toll on university research labs across the country. Students and scholars from other countries who have applied to study or train in the US have encountered delays of weeks or months and even outright denials. Even foreigners who have worked in the US for years are running into trouble. Researchers complain that projects go untended, cultures die and data is lost when their lab members are unable to return from a trip home.

MCB is no exception. A quick poll of the department turned up at least a dozen labs that have encountered visa problems recently. Some preferred not to have their names used in this article for fear of attracting unwanted attention from immigration officials. Others agreed to tell their story. Here are three.

Stuck in China

Zhiyuan Yang was supposed to have started in the MCB graduate program last fall. He first came to Berkeley in 1999 after graduating from Xiamen University in Fujian Province, China. As a visiting scholar with Biochemistry and Molecular Biology associate professor Qiang Zhou, Yang identified a small nuclear RNA that regulates HIV gene expression. The finding was published in *Nature* in 2001 (vol. 414, pp. 317 – 322).

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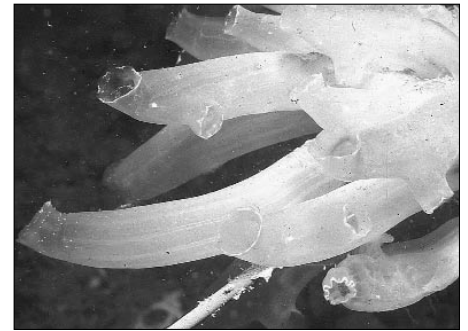
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and you block the limb. Move it somewhere else, and you can get a limb somewhere else too. Changing the expression pattern of *Ultrabithorax* (*Ubx*) in flies can convert halteres to wings, producing a more dragonfly-like arrangement. While this may not be how four-winged insects arose, it is clear that regulatory changes are a powerful generator of variation, and evolution has taken full advantage. So to understand how diversity has evolved, we need to understand the regulatory DNA—the regions of the genome that control gene expression, and the protein factors that bind to them.

The link to diversity was a primary attraction for the Moore Foundation, says Ed Penhoet, former dean of the School of Public Health and a co-founder of Chiron Corporation in Emeryville, who now directs

menagerie over the years. Besides fruit flies, he has studied grasshoppers, flour beetles, crickets, shrimp and lobsters. His group's experiments have shown how differences in the expression pattern of developmentally important genes discovered in the fruit fly underlie the different body plans of various arthropods. In crustaceans, for example, the expression boundaries of the homeobox genes *Ubx* and *abdominal-A* determine where the mouthparts end and limbs begin.

Now Patel has a new crustacean in the lab known by its Latin name, *Parhyale hawaiiensis*. His hope is that *Parhyale* will become a standard laboratory representative of crustaceans for evo-devo questions, just as the frog *Xenopus laevis* represents amphibians and the mouse represents mammals. Among *Parhyale's* advantages is its highly organized



Missing Link:

The sea squirt has features in common with both vertebrates and invertebrates.

Aquarium, where it was clearly tolerating a wide variety of conditions. "We knew it was something that didn't require a lot of care," he says. Like fruit flies, nematodes and mice, *Parhyale* can essentially live on garbage.

Another creature that will feature at the CIG is the sea squirt (*Ciona intestinalis*). A sessile organism that favors rocks and ship hulls, the sea squirt has long intrigued biologists. The tubular adult is an invertebrate, but the swimming tadpole larva has a notochord. This rare combination convinced Charles Darwin that vertebrates and invertebrates must have a common ancestor.

Today, *Ciona* may still be the key to unlocking the story of vertebrate evolution, as several features make it amenable to study. It has relatively small genome—120 Mb or a mere 4% the size of the human genome; it has simple cell lineages, much like the nematode; and DNA can be electroporated into its cells. In December, JGI announced that *Ciona* had become the seventh animal to have its genome completely sequenced.

Parhyale's genome—about 5 times bigger than the fruit fly—may not be done quite so quickly. But Patel hopes to begin by sequencing collections of DNA known as expressed sequence tags (ESTs), which represent expressed portions of the genome. For this purpose, the nearby sequencing power of the JGI will come in handy.

Also critical will be the bioinformatics expertise on the CIG faculty. Among the experts is Daniel Rokhsar, a condensed matter physicist who has remade himself into a bioinformatics guru. As associate director for computational genomics at JGI, Rokhsar has been a lead investigator on important sequencing projects such as the pufferfish and the sea squirt. He joined the MCB faculty this spring. Also on staff at CIG is Gene Myers, a Professor of Computer Science and a developer of a variety of computational tools including BLAST, the widely-used



Genetics & Development Professors Michael Levine (pictured) and Richard Harland will co-direct the Center for Integrative Genomics.

the foundation's science and higher education programs. Much of the foundation's work is in the area of biodiversity and conservation, which necessarily includes the evolution of diversity, Penhoet says. "There will be a finite number of gene families, and how they are expressed both spatially and temporally is a very important driver of evolution. It defines diversity." The foundation's grant was announced in November and will be spread over 5 years.

One of the leaders in evo-devo research is Nipam Patel, who has accepted a position in MCB and will join the CIG this summer (see profile p. 3). Patel has dealt with quite a

development. At the 8-cell stage, each cell is a founder for one of the three germ cell layers—ectoderm, endoderm and mesoderm. Also, cells of the *Parhyale* embryo survive injections just fine, and RNA interference (RNAi), which blocks expression of specific genes, appears to work. Patel's group has already found they can knock down a gene on one side of the animal by injecting RNA into one cell after the first division. They are also working on a way to genetically transform the animal with transposable elements.

And quite importantly, *Parhyale* is easy to grow. In fact, Patel found it in the filtration system of Chicago's famous Shedd

protein similarity search engine. As vice president of informatics at Celera Genomics in Rockville, Maryland, Myers wrote the code that assembled the human genome from millions of shotgun-sequenced fragments.

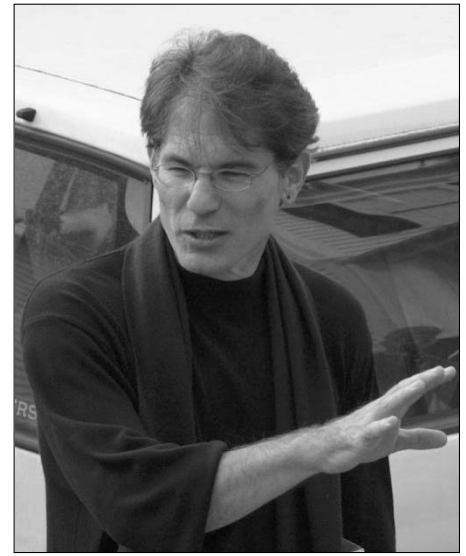
That computational brain trust will be critical to a second goal of the center—to develop and implement an annotated sequence database, a sort of hyper-Genbank. Whereas Genbank currently houses all the public data, it is weak on genome assemblies. Sometimes it can be hard to tell whether two genes are on the same chromosome, for example. It also has limited user-friendliness, and of course it lacks any significant annotation on regulatory sequences. The CIG's database would improve on Genbank by giving researchers a simple way to access both kinds of information. In addition, it should be absolutely intuitive to use, says Levine, who is co-directing the center with G&D Professor Richard Harland. "We want a very simple, graphical site of DNA assemblies.

It's got to be easy for any biologist to use," Levine says.

For graduate and post-doctoral training, the center will be a huge boon. Successful future genomicists will need a rare combination of experience, including computational training, evolutionary biology and embryology. With its cross-disciplinary faculty, already 19 strong, the Center for Integrative Genomics is the perfect place for people interested in genomics to train.

And interest is high, as evo-devo and genomics are shaping up to be among the most exciting areas of biology. Where might it all lead? "The day will come when you can read off the sequence and deduce the organism," Levine speculates. Imagine a computer program that can digest raw DNA sequence and compute the product—a llama, or a trumpetvine, or a gnu. Brave new world indeed.

Website: <http://mcb.berkeley.edu/cig/>



Gene Myers helped assemble the human genome.

NEW FACULTY



Nipam Patel

Most of what we know about embryonic development at the molecular level has come from a small number of model organisms, principally frogs, fruit flies, nematodes and mice. But all along in the back of biologists' minds has been a nagging worry. What if the animals we have studied in such detail turn out to be the exception, rather than the rule? What if they are not representative of life?

A little more than ten years ago, a handful of molecular biologists began looking at a wider variety of organisms, in part with the aim of learning whether the genes and processes discovered in common lab animals figured in the development of other species. Nipam Patel was at the forefront of this effort.

As a graduate student in Corey Goodman's lab at Stanford and Berkeley in the late 1980's, Patel became one of the first to clone the homologs of important fruit fly development genes from other insects. He found that the genes were in fact highly conserved, but played different roles in different

insects, depending on the pattern of development.

Since then Patel has become a leading researcher in the study of the evolution of development, also known as evo-devo. As a professor at the University of Chicago and an associate investigator in the Howard Hughes Medical Institute, he has gathered crustaceans in Belize, spiders in Chicago, and butterflies in Africa in his effort to tease out the evolutionary history of embryogenesis.

This summer he joins the department as a full professor and as one of the linchpins in the new Moore Center for Integrative Genomics (for more, see page one). All five of his graduate students, three postdocs, and one of three technicians are making the move with him. He says he is looking forward to the tremendous resources Berkeley and the Bay Area have to offer, including the strong developmental biology community and the sequencing power and genomics expertise of the Joint Genome Institute and the Lawrence Berkeley Labs.

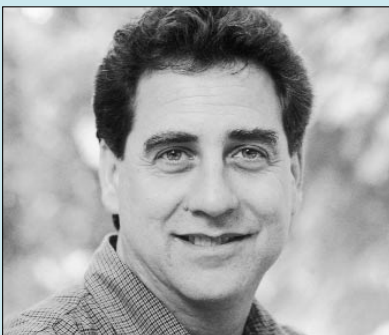
FACULTY NEWS

Lu Chen (Neuro) received a Beckman Young Investigator award from the Arnold and Mabel Beckman Foundation.



▲ **Ehud Isacoff** (Neuro) was appointed to the Class of 1943 Memorial Chair.

Caroline Kane (BMB) was the Frontiers in Science Distinguished Invitrogen Lecturer at the University of Buffalo in February, sponsored by both the Buffalo Department of Biological Sciences and the Department of Microbiology. She gave two seminars and says she had a great and productive time. Also this Spring she was awarded the Phi Beta Kappa Northern California Association Award for Teaching Excellence and the 2003 Judith Pool Award from the Northern California Chapters of the Association for Women in Science given for making a significant effort to advance others in their careers.



▲ **Daniel A. Portnoy** (BMB) has given three invited lectures recently: He took part in the Distinguished Scientist Lecture Series

at the University of Pittsburgh School of Medicine in April. In January he gave the Willison Memorial Lecture for the Department of Microbiology & Immunology at the University of Michigan. And in November he participated in the Lansdowne Lectures at the University of Victoria.



▲ **Jasper Rine** (G&D) gave the Gabriel Lester Memorial Lecture at Reed College in January.

Gerry Rubin (G&D) was elected to the Institute of Medicine of the National Academy of Sciences. He also shared the 2003 Beadle Award with Allan Spradling of the Carnegie Institution of Washington. The award is given by the Genetics Society of America for outstanding contributions to the genetics research community. Rubin is currently on administrative leave to serve as Vice-President and Director of Planning for the Howard Hughes Medical Institute's Janelia Farm Campus in Ashburn, Virginia. Website: www.hhmi.org/janelia/

Jeremy Thorner (BMB) gave an invited talk at the Juan March Institute in Madrid in January for a symposium entitled "Membranes, Trafficking and Signaling during Animal Development." For the purposes of this meeting, he says, yeast was considered an honorary animal.



▲ **Matthew Welch** (CDB) received an Established Investigator Award from the American Heart Association.



▲ **Qiang Zhou** (BMB) was promoted to the rank of associate professor last July.

Division Abbreviations:

BMB, Biochemistry and Molecular Biology;
CDB, Cell and Developmental Biology;
G&D, Genetics and Development;
Immuno, Immunology;
Neuro, Neurobiology.



Erlinda Aquino

1961–2002

Erlinda Aquino, the much-loved laboratory assistant in the Koshland Hall media facility, died on December 20 at her parents' home in the Philippines after a 3-year battle with breast cancer. She was 41.

Aquino joined the department in 1988 as a laboratory assistant for John Clark in Stanley Hall. After Koshland Hall was completed in 1990, she was asked to take charge of the weekly fly food supply for the new building. She also made up essential solutions and culture media for Koshland Hall's 13 MCB laboratories. Over the years, Aquino made many friends in the department, and her consistently cheerful and competent work earned the respect and appreciation of all those who relied on her.

Despite her illness and several debilitating rounds of chemotherapy, Aquino worked on and off until 3 months before her death. She is survived by her 11-year-old son Michael.



Barroso: A trip home for Christmas became a 2-month ordeal.

The department granted him admission to the graduate program for Fall 2002, and Zhou guaranteed him a spot in his lab. But Yang had to return to China to renew his J-1 visa. Despite having been admitted to Berkeley, his application was refused. He has since tried again twice, with the same result. He says the US visa office doesn't believe he will return to China after his studies are complete.

For now he is doing research on antiviral mechanisms in shrimp at the Third Institute of Oceanography in Xiamen. This summer, he will apply again. "I want to begin my graduate work as soon as possible," he wrote in an e-mail, "but it really doesn't depend on me."

Forced Vacation

When Consuelo Barroso, a postdoc in David Drubin's lab, left for Spain in the middle of December, she thought she was just going home for Christmas. But it was not to be.

Although she needed an extension of her visa to return, she had prepared everything in advance—the proper forms and a letter detailing the purpose of her stay. It should have been routine. "I checked," says Barroso, "people have been doing this for many years."

But when she visited the US embassy in Madrid in December, they said wait would be at least two weeks. Later, they asked her for more information and a letter from her advisor. In the end, she didn't get back to Berkeley until March.

It might not have been so bad, except that there was no computer at her family's house, and it was hard to keep in touch with the lab. By the time she got back, she felt completely out of it, she says. "You are gone for so long you forget what you were doing."

Just Wait 3 Years

Aria Eshraghi barely made it to Central America this spring. A junior working on his honors thesis in Bruce Ames' lab, he was accepted to a study-abroad program at the Monteverde Biological Station in Costa Rica back in November. American citizens can travel freely to Costa Rica, but Eshraghi is not a citizen of any country. His family fled Iran in 1982 and soon after sought asylum in the US. Eshraghi is a permanent resident, but does not yet have citizenship. So he contacted the INS immediately after hearing of his acceptance and applied for the necessary travel documents.



After hearing nothing for 3 months, he began to get nervous. The INS customer service agents assured him the documents would arrive within weeks. But they didn't. With a bit of sleuthing, Eshraghi worked out that the office handling his application was in Nebraska. They gave him a different estimate of the delay: about 3 years.

Now very nervous, he went to his local congresswoman, Lynn Woolsey, who assigned him a caseworker to expedite his case. A few weeks later, the documents arrived—only this was now two days after the program in Costa Rica had begun. It took only a week to get a visa from Costa Rica, but by the time he finally arrived, he had missed a fifth of the classes. It will be difficult to catch up, he says, but his instructors have been very understanding.

STUDENT AWARDS

UNDERGRADUATE

AWARDS

- University Medal Finalist – Anosheh Afghahi (Kuypers Lab at CHORI)
- MCB Department Citation – Anosheh Afghahi

Division of Biochemistry and Molecular Biology

- Grace Fimognari Memorial Prize – Amie Lee (Jablons Lab at LBNL)
- Kazuo Gerald Yanaba & Ting Jung Memorial Prize – William Ridgeway (Cate Lab)
- F.H. Carpenter Memorial Prize – Margaret Chow (Kirsch Lab)

Division of Cell and Developmental Biology

Chaikoff Memorial Awards

- Bobby Lut-Ming Tsang (Meyer Lab)
- Saori Lillian Haigo (Harland Lab)
- Joseph Younghan Kim (Firestone Lab)
- Henry Omobolaj Ade Ola Delu Jr. (Anthony DeFranco lab at UCSF)
- Jennifer Reth Giampaolo (Firestone Lab, also a Beckman Scholars Program awardee)
- Omar Saeed (Timiras Lab)
- Wai Cheong (Vreeland Lab at LBNL)
- Eugenia Yunju Kim (Campisi Lab at LBNL)

Division of Neurobiology

Chaikoff Memorial Awards

- Darya Lee Pino-Dempsey (D'Esposito Lab)
- Anahita Jaffari (Miller Lab)

Division of Genetics and Development

- Spencer W. Brown Award – Gregory Havlena (Drubin Lab) and Wendy Lam (Kaufman Lab)

Division of Immunology

- Outstanding Undergraduate – Louis Savar (Schlissell Lab)

GRADUATE AWARDS

- Iain Cheeseman (Barnes Lab) was one of sixteen graduate students from North America and Europe who have been selected to receive the 2003 Harold M. Weintraub Graduate Student Award, which is sponsored by the Basic Sciences Division of the Fred Hutchinson Cancer Research Center. Cheeseman now goes on to a postdoctoral fellowship at the Ludwig Institute for Cancer Research in San Diego.

The following MCB students have received graduate fellowships from the National Science Foundation.

- Brian Carlson (Bertozi Lab)
- Shirley Huang (Incoming Class)
- Carolyn Phillips (Dernberg Lab)
- Allyn Schoeffler (Incoming Class)
- Jennifer Zeitler (Bilder Lab)

OUTSTANDING GRADUATE STUDENT INSTRUCTORS

The following graduate students who taught MCB courses were selected as this year's Outstanding Graduate Student Instructors.



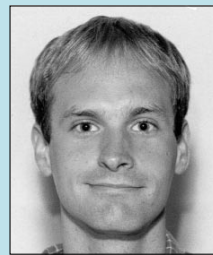
▲ Annie Lee (Meyer Lab)



▲ Kim L. Failor (Firestone Lab)



▲ Carla DiGennaro (Rio Lab)



▲ John Gladden (Meyer Lab)



▲ Timothy Kutzkey (Tjian Lab)

- Michael Lai (School of Public Health)
- Suzanne Lee (Collins Lab)
- Catherine Seeley (School of Public Health)



▲ Bryan Zeitler (Weis Lab)



▲ Jennifer Zeitler (Bilder Lab)

CLASS NOTES



BA 1990

■ **Henry G. Chun**, M.D., did a 3-year internal medicine residency at Highland Hospital in Oakland, where he was chief resident. He went on to a gastroenterology fellowship at New York University Medical School, Northshore University Hospital. He will be a gastroenterologist at Kaiser Permanente in Richmond, California, this fall.

BA 1992

■ **Gregory A. Montoya** writes that he has put off material and economic gain to observe the “living and inanimate aspects necessary for the maintenance of the world”. He says he has travelled widely, hiked deserts and climbed mountains on a quest for spirituality. His e-mail is roadscholar@cal.berkeley.edu

BA 1993

■ **Paul Woo** is a product manager at Protein Design Labs, a biotech company in Fremont that develops humanized monoclonal antibodies for cancer, autoimmune and inflammatory diseases. After graduating from MCB, he joined Gary Firestone’s lab as a graduate student in endocrinology where he studied glucocorticoid regulation in mammary tumor cells. He received his Ph.D. in 1999. He worked at a marketing consulting firm for about a year before going to PDL. E-mail: plwoo@hotmail.com

BA 1995

■ **Bryant E. Fong** is a director at Burrill & Company, a San Francisco-based venture capital firm investing in biotechnology. He has been making investments for more than four years now, and has had several successful IPOs. E-mail: bryant@b-c.com

■ **Benjamin Sebastian Santos** is a 2nd-year medical student at the UC Davis School of Medicine. After Cal, he earned a Master’s of Public Health with a major in Epidemiology. He worked for Kaiser Los Angeles, UCLA and Children’s Hospital Los Angeles before starting medical school. E-mail: bssantos@ucdavis.edu

BA 1996

■ **Laura McDevitt** is a Senior Associate QA Development Scientist at Bayer Corporation. She asks anyone interested in the East Bay Chapter of the Association for Women in Science to please contact her at lauramcdev@hotmail.com.

BA 1998

■ **Holly Chang** has returned to graduate school. Before coming back she spent two years in healthcare consulting and two years at ePocrates (medical technology

continued on back page. . .

CLASS NOTES WANTS TO HEAR FROM YOU

Do you have a BA, MA, PhD in Molecular and Cell Biology from Berkeley? Have you recently changed jobs, schools, or countries? Here is an easy way to let your classmates know what you have been doing and maybe reconnect with old friends. Send your class note for the next issue.

It’s so easy. You can:

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startup company in the Bay Area). She is now a first-year MBA student in the healthcare management program at Wharton. After school, she hopes to work in public health in Los Angeles. Email: hollychang@yahoo.com.

BA 1999

■ **Nagina Sethi** is Strategic Project Manager for Kaiser Vallejo Hospital, as well as outpatient clinics in Fairfield, Vacaville and Napa. Sethi manages strategic initiatives and new programs. Before that, Sethi did strategic planning and program planning

for the Northern California region for Kaiser Permanente's management consulting group. Sethi snowboards and lives in Oakland. E-mail: nagina_77@yahoo.com

Ph.D. 1994

■ **Myung K. Shin** has been an associate member in the Cellular and Developmental Biology Program at Fox Chase Cancer Center in Philadelphia since September, 2000. Shin was named a Pew Scholar in 2001 by the Pew Scholars Program in the Biomedical Sciences. E-mail: MK_Shin@fcc.edu

Ph.D. 1996

■ **Lubor Gaal** heads a Marburg-based biotech company, Vectron Therapeutics, which develops targeted cancer therapies. He left Berlex Labs in New Jersey in September 2001 and has been living in Germany since. Although he never looks back to academia, he does have fond memories of life in the Bay Area and hopes to enjoy it again someday. E-mail: gaal@vectron-ag.com

Postdocs Unite!

Berkeley reaffirmed its tradition of incubating grassroots movements in March when the campus hosted the inaugural meeting of the National Postdoctoral Association (NPA). With a generous grant from the Alfred P. Sloan Foundation and sponsorship by the American Association for the Advancement of Science (AAAS), the group seeks to improve the lot of the postdoctoral researcher. The NPA's plans include providing information on compensation and other policies at institutions around the country and hosting a career website for postdocs.

UCSF biologist Keith Yamamoto, the keynote speaker at the March 15 meeting, said postdoctoral training too often serves as a "holding pattern" for scientists who may be as likely to branch into other careers in business or law as to continue in research. Policies that promote an earlier branch point would reduce the number of postdocs and improve the career prospects for those who chose academia, Yamamoto said.

Those interested in joining the NPA can find them on the internet at www.nationalposdoc.org.

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