2012

MCB TRANSCRIPT

Spring/Summer 2012 Volume 15, Number 1

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

Flexible Connections:

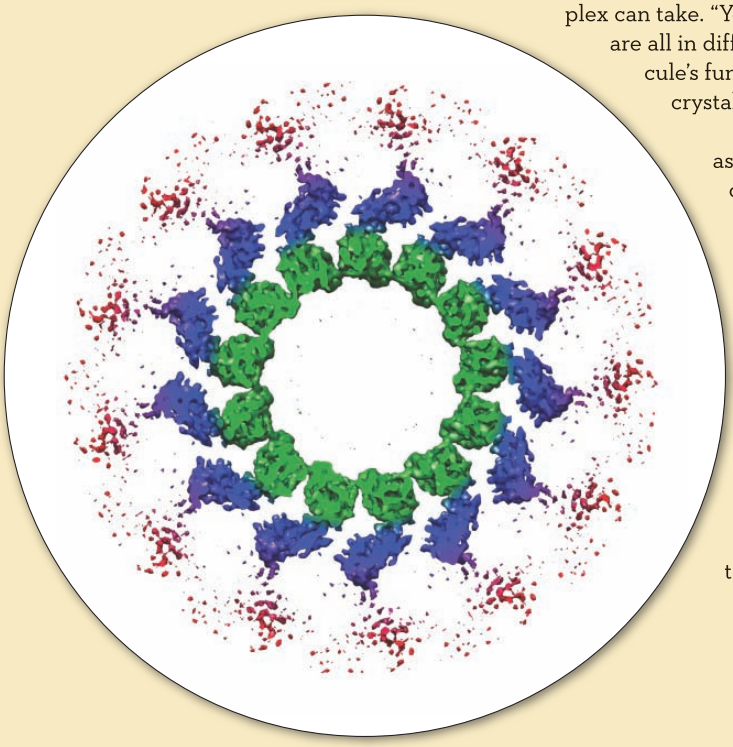
How Microtubules Pull Chromosomes Apart

When cells divide, microtubules pull the replicated chromosomes apart to make sure each daughter cell gets a full set. To do this, microtubules attach to the sister chromatids via a protein structure called the kinetochore. "How do microtubules sense when the kinetochores on both chromatids are attached?" asks MCB Professor Eva Nogales. "It's very bad if they pull too soon."

A key to this question is the Ndc80 complex, a protein assemblage in the kinetochore that links microtubules to chromosomes and that is conserved in organisms from yeast to people. Using a technique called cryo-EM, Nogales takes "snapshots" of Ndc80 complexes that were flash-frozen while in action. "They're frozen so fast that water doesn't even form ice," says Nogales, who is a biophysicist and chairs the Biophysics Graduate Group.

Collectively, these snapshots reveal the natural range of shapes the complex can take. "You get a population of many identical molecules that are all in different conformations that are relevant to the molecule's function," she says. This is because, in contrast to X-ray crystallography, cryo-EM starts with molecules in solution. This makes cryo-EM ideal for systems that self-assemble, such as microtubules and other cytoskeletal components. The technique also lends itself to large complexes that are flexible or rare in the cell, both of which are difficult to study with x-ray crystallography. "Flexible complexes won't crystallize, and crystallography needs a lot of material," says Nogales. "With cryo-EM, you can get a lot of information from a small amount of material."

To get a more complete picture of how the Ndc80 complex works, Nogales combined cryo-EM-derived structures with those yielded by other imaging techniques. "The challenge is to ask a well-defined biological question and choose the methods that will best answer it," she says. "You have to combine them in clever ways."

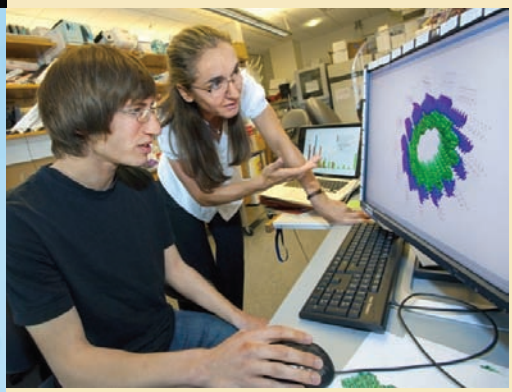


Cryoelectron microscopy reconstruction of an end-on view of the microtubule–Ndc80 complex interface (tubulin, green; Ndc80 complex proteins, blue, red). Photo: Nature

Continued on page 2 >

Flexible Connections continued from page 1 >

MCB Professor Eva Nogales
Photo: Paul Fetters for HHMI



Eva Nogales and graduate student Greg Alushin discuss his work on how the Ndc80 complex interacts with microtubules.
Photo: Roy Kaltschmidt for LBNL

The Ndc80 complex includes four proteins, and the structure of each of these was already known from x-ray crystallography. Nogales' lab then used electron tomography, which yields low-resolution images of single objects, to see how individual Ndc80 complexes behave on the microtubule surface. Her team also used 3D-reconstruction of cryo-EM, which builds higher-resolution images by averaging many objects, to see how Ndc80 complexes interact with microtubules.

By using cryo-EM on human Ndc80 complexes that were attached to microtubules, her team discovered something new about how this protein assemblage works. The complex has a tail that is required for binding to tubulin, the protein that makes up microtubules. However, the mechanism of this tubulin binding was unknown. Nogales' team found that when Ndc80 tails are dephosphorylated, clusters of complexes line up on and stick to adjacent tubulin subunits in microtubules. This is because the tails flip from sticking out from the complexes to nesting between them and attaching to tubulin subunits. "The tail is like cement between complexes," she says. "We got the function and regulation from being able to visualize it directly." The tail's role in the self-assembly of Ndc80 complexes on microtubules would have been impossible to learn from more conventional methods such as x-ray crystallography. "The tail is functionally essential, but it won't crystallize because it's flexible," says Nogales. "You have to chop it off to do crystallography."

The Ndc80 tails are not dephosphorylated until microtubules contact the kinetochores on both sister chromatids. Once that occurs, the microtubules start losing tubulin subunits from the kinetochore end. Because the kinetochores still remain attached to the shrinking microtubules, they pull the chromatids to opposite sides of the soon-to-divide cell.

How do the kinetochores stay connected to microtubules where tubulin subunits are popping off like beads? The answer is that the kinetochores are attached to the clusters of Ndc80 complexes. But of course this just shifts the question to the Ndc80 complexes. So how do these protein assemblages stay connected to microtubules that are in the process of breaking down? Microtubules curve outward before depolymerizing, bending at a hinge between subunits and so nudging the Ndc80 complexes further down their length. "The complexes slide away from the curve but still remain attached," says Nogales.

The next step is characterizing the Ndc80 tail more fully. "It has many roles ," she says. "We're coming very close to cracking it."

Bound Biomolecules:

Catching Proteins and Molecular Motors in Action

Molecules in our cells are constantly in motion, from proteins that fold and unfold to molecular motors that make RNA, DNA and proteins. To catch molecules in action, MCB Professor Carlos Bustamante holds them in place with a technique called optical tweezers. "This method exploits the fact that light, when focused into a small spot, can trap pieces of matter," he says.

In his lab, the matter trapped by optical tweezers is a tiny polystyrene bead that is connected to one side of the molecule they want to study. The other side of the molecule is connected to a fixed surface, typically another bead that is held in place by a miniscule pipette. Bustamante and his students use this approach to study the behavior of individual biomolecules.

Besides tethering molecules, optical tweezers can tug at them, thus stretching them between the two beads. This makes optical tweezers ideal for investigating protein folding and unfolding. "Applying mechanical force is more biologically relevant than denaturing proteins with urea or temperature," says Bustamante, a biophysicist who is also a member of the Biophysics Graduate Group. "The cell uses enzymes called unfoldases that grab a protein at one end and pull it for targeted unfolding." Proteins targeted for unfolding include those down-regulated at various points in the cell cycle as well as those that have been modified so that they are no longer useful. Understanding protein folding and unfolding is important partly because misfolded proteins can form amyloids, which are implicated in neurodegenerative disorders such as Alzheimer's and Parkinson's diseases.

One protein that Bustamante's lab focuses on is a lysozyme from the bacteriophage T4, which is the most extensively studied for protein folding. "We grab the protein as it's coming out of a ribosome and use optical tweezers to unfold and refold it," he says. This lets them address the question of why new proteins don't misfold as they are being made, which is intriguing because proteins can fold much faster than they are synthesized. His lab found that ribosomes help new protein fragments fold properly. Optical tweezer studies showed that when fragments of new proteins are isolated in solution, misfolding is common. But when these fragments are left on the ribosome, folding is slower and more accurate. "The ribosome acts as a chaperone that keeps the protein from pre-folding," says Bustamante.

Professor Carlos Bustamante
Photo: LBNL

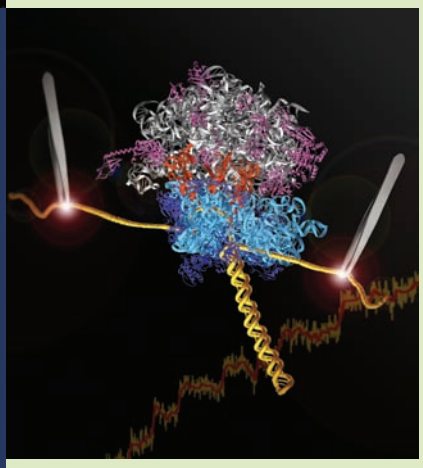


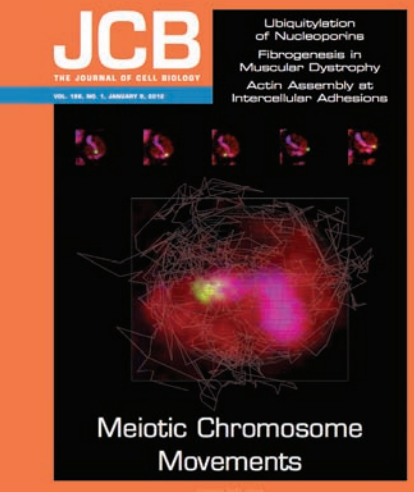
Illustration of a ribosome caught in optical tweezers against a force graph showing that ribosomes pull mRNA through themselves three bases at a time.
Photo: Nature

Likewise, his lab uses optical tweezers to follow molecular motors as they work. "The cell is full of molecular machines that couple the energy from chemical reactions to mechanical tasks," he says. For example, in viruses and bacteriophages with protein coats (capsids), a molecular motor at the capsid base packs the DNA efficiently inside. Bustamante's lab found that bacteriophage motors have a ring of subunits with moving parts that work together to catch onto and push the strand of DNA into the capsid. Placing a small tracking bead on the DNA showed that it rotates during this process, resulting in neat coils inside the capsid. "This is the highest resolution model of how a molecular motor works step-by-step," says Bustamante.

Another optical tweezer study revealed that RNA polymerase moves DNA through itself during transcription, leading to the question of what happens when this enzyme meets one of the many nucleosomes that DNA wraps around. "Does the RNA polymerase stop? Does it bump the nucleosome out of the way?" asks Bustamante. It turns out that RNA polymerase takes advantage of the fact that the nucleosome and the DNA naturally come apart periodically. The RNA polymerase stops and sits, waiting for the nucleosome to separate from the DNA. And then it advances. This sequence of events is repeated all along the nucleosome as successive parts of it separate from the DNA.

When tethered and then tugged at by optical tweezers, ribosomes can still translate mRNA against that force. By measuring changes in force during translation, Bustamante's lab found that like RNA polymerase, ribosomes pull mRNA through themselves—and that they pull three bases (that is, one codon) through at a time. Now that translation can be followed codon by codon, Bustamante wants to get a similarly close look at protein synthesis by following a polypeptide chain coming out of a ribosome as it is translating. "Single molecule experiments can give us a unique look into molecular mechanisms," he says. "It's pretty amazing what it's possible to do these days."

Professor
Abby Dernburg



After pairing, chromsomes zigzag vigorously around the nucleus, presumably to trigger synapsis.

Meiosis in Motion:

Watching Chromosomes Form Matched Pairs

In meiosis—the type of cell division that produces eggs and sperm—chromosomes from each parent form matched pairs, enabling the crossing over that results in genetic diversity. But how do chromosomes find the right match and then how do they stick together? "You can't really study this in culture–it has to be in the whole animal," says MCB Professor Abby Dernburg. This used to mean inferring the steps of meiosis from fixed samples at different stages of the process. But no more. "We've recently moved into live imaging," she says.

It helps that her model organism, the nematode *Caenorhabditis elegans*, is completely transparent. In addition, her lab is using techniques that push the boundaries of 3D imaging in living animals. This imaging involves the summation of optical "slices" through nematode gonads. Right now her lab gets 3D images at 30-60 second intervals and their goal is to bring that down to every 10 milliseconds. This involves first making a series of 2D images of optical "slices" through a nematode gonad, and then summing those slices to make a 3D image. Because summation is such a slow process, right now her lab only gets 3D images at 30-60 second intervals. But their goal is to bring that down to every 10 milliseconds. "We want to watch biology live," says Dernburg.

One challenge is that meiosis takes a few hours in nematodes but keeping them under microscope light that long can be harmful. Moreover, fluorescent tags bleach during imaging. "They disappear as you watch them," says postdoctoral researcher Ofer Rog. Both issues are addressed by confining the illumination to the "slice" being imaged and by keeping the light low. Getting the most out of these low-light images requires a technique called computational denoising. "You can get information that doesn't even look like it's there," says Dernburg.

To follow chromosomes as they pair in the gonads of living nematodes, Rog and other lab members put red fluorescent tags on X chromosomes and green fluorescent tags on a protein that binds the chromosomes' pairing centers. Called HIM-8, this protein also connects X chromosomes through the nuclear envelope to microtubules in the cytoskeleton. Powered by molecular motors called dynein, the microtubules move chromosomes around during the process of cell division. Live imaging showed that chromosomes pair almost immediately after cells enter meiosis. In addition, chromosomes go from hardly moving before pairing to zigzagging around the nucleus afterwards.

The team also found that dynein motors are not needed for chromosome pairing. "We think they pair by random collisions and that once paired properly, they join together in synapsis," says Rog. In contrast to pairing, dynein may be critical to synapsis. "Dynein yanks the chromosomes so quickly and forcefully that they go from one side of the nucleus to the other in just a few seconds," says Rog. This vigorous yanking may help the right pairs align and keep wrong pairs apart. The yanking continues until synapsis is complete, which takes about two hours. "Somehow, the nucleus can tell when it still has unpaired chromosomes," says Dernburg.

Rog is now looking at the synaptonemal complex that holds the aligned chromosome pairs together. "Does it work like a zipper, starting at one end and going along the chromosome, or does it start in multiple spots?" he asks. "This is the kind of question we're getting closer to solving."

Biophysics graduate student Keith Cheveralls is studying another aspect of synapsis. "One of the key mysteries of meiosis is how the number and position of crossovers is regulated," says Dernburg, who is also part of the Biophysics Graduate Group. In nematodes, each chromosome gets just one crossover and the mechanism for transmitting the information that this has occurred chromosome-wide is unknown. It could be that crossing over decreases the chromosome's tension, thereby changing its shape. To test this, Cheveralls is studying the conformation of synapsed chromosomes. "Are the squiggles random or biologically significant?" he asks.

Ultimately, Dernburg hopes to investigate meiosis using single-molecule imaging techniques. "If we can reconstruct the key events of meiosis, we may be able to study them with, say, optical tweezers," she says.

Fine Filtering:

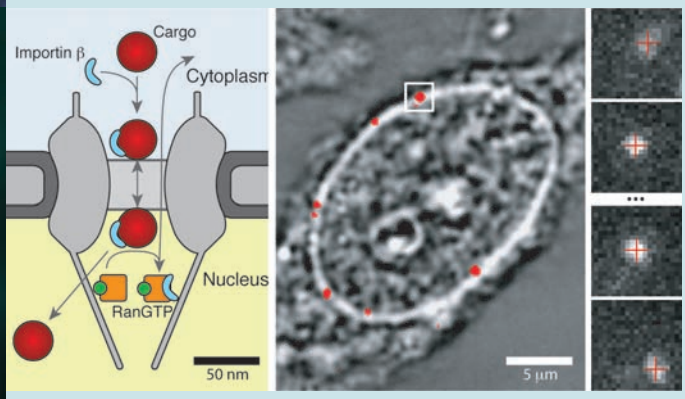
Tracking Nuclear Transport

Professor Karsten Weis

Materials go in and out of the nucleus at an amazing rate, for example with proteins entering and RNA exiting. "Every minute, millions of molecules are transported," says MCB Professor Karsten Weis. "It's energetically costly." These exchanges between the nucleus and the cytoplasm are mediated by the nuclear pore complex and Weis has recently gotten a close look at its inner workings, thanks to single-molecule imaging studies in collaboration with UC Berkeley Physics Associate Professor Jan Liphardt.

The nuclear pore complex (NPC) is a gigantic assemblage of proteins that spans the nuclear envelope, controlling what gets imported and exported. "It's exquisitely selective, which is great for regulating gene expression," says Weis. The NPC has also been implicated in aging and diseases including leukemia. The nuclear envelope typically has 2,000 to 4,000 NPCs and once assembled, they are quite stable. "The cell doesn't seem to break them down or turn them over," says Weis. "It appears that oxidative damage with age makes them less selective, which would be damaging to the cell."

The NPC's enormous size makes it hard to study. "It's 30 to 40 times bigger than a ribosome," says Weis. "We haven't been able to assemble it *in vitro*." To find out how the NPC works, his lab simplifies mammalian cells by punching holes in their membranes with detergent, washing them out, and then adding individually-labeled components back in. This lets the research team track single molecules through the pore and into the nucleus.



Left: Illustration of a quantum dot traveling through the NPC.
Center: A single quantum dot (in red and boxed) the nuclear envelope.
Right: Consecutive images of the quantum dot arriving from the cytoplasm (top), traveling through the NPC (middle), and departing into the nucleus (bottom).
Photo Left: unpublished
Photo Center and Right: Nature

To get a better view of the pore, Liphardt helped Weis track light-emitting semiconductor materials called quantum dots through individual NPCs. "The beauty of quantum dots is that they are very bright, much brighter than GFP," says Weis. GFP (green fluorescent protein) also has the drawback of bleaching with time. To get the NPC to import quantum dots, the team tagged them with an amino acid sequence called nuclear localization signal that directs compounds into the nucleus.

Another benefit of quantum dots is that they are so big that they travel through the pore slowly. Previous imaging work used small proteins that zoomed through in milliseconds, too fast to see the details of how they were transported. In contrast, "it can take seconds for quantum dots to go through so you can see all the substeps as they meander through the pore," says Weis. Although large, these quantum dots are close in size to other transported materials like pre-ribosomal particles and viruses. "We think our findings are biologically relevant," he adds.

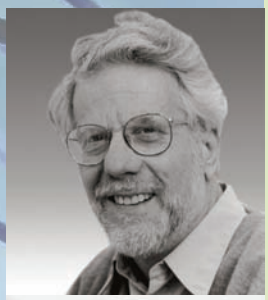
In combination with previous work, the quantum dot tracking studies suggest that NPC transport involves at least three steps. The first is regulating entry into the pore with a size-selective filter. "Quantum dots that are bigger than 40 to 50 nanometers can't get in," says Weis. "They're rejected at a certain position and we think that's the location of the size filter." This conclusion is supported by a composite of all the individual quantum dot trajectories through the pore, which yields a cloud suggesting an hourglass-shaped channel. "This reveals the maximum diameter of the channel," says Weis, pointing out that this filtering by size does not require energy.

The same holds for the next step of getting the molecule through the pore. Images of the slow-moving quantum dots revealed that once inside the pore, they take random trajectories through it. "They bounce around stochastically," says Weis. "The cell doesn't use energy to do this either."

The final step of actually entering the nucleus is the only part of the transport process that uses energy. After reaching the pore's nuclear end, the receptor that transports molecules must bind a GTPase before they can be released into the nucleus. Interestingly, Weis's lab had previously shown that switching this GTPase from one end of the pore to the other also reverses the direction of transport. This fits with the quantum dot study finding that molecules move through the pore randomly. "It was great to see that the NPC itself doesn't provide directionality," he says.

Weis's collaboration with physicist Jan Liphardt has transformed his understanding of the NPC. "The great thing about this campus is there are people with fantastic expertises in all areas so we can address our big questions with physics and biology," he says. "Jan and I each got excited about the project so we had great synergy—neither of us could have pulled it off alone."

FACULTY NEWS



CARLOS BUSTAMANTE won the 2012 Vilcek prize, which recognizes outstanding contributions of foreign-born scientists and artists living and working in the United States. The artist recipient for the prize was ballet dancer Mikhail Baryshnikov.

MICHELLE CHANG and **MING HAMMOND** are recipients of the 2011 NIH Director's New Innovator Award.

DAN FELDMAN was on sabbatical at Institute Pasteur for Fall 2011, where he began work on a textbook on the brain's cerebral cortex. He was a Heller Distinguished Lecturer at Hebrew University, 2011.

MARLA FELLER was on sabbatical at Institute Pasteur for Fall 2011. While there, she piloted experiments on the role of dendritic integration in retinal processing using state of the art imaging methods in David DiGregorio's lab. She received the École des Neuroscience of Paris sabbatical award, 2011, and was a Heller Distinguished Lecturer at Hebrew University, 2011.

POLINA LISHKO received a grant from the Winkler Family Foundation for the purpose of supporting the research of an innovative young faculty member. She has also been selected to speak in the New and Notable Symposium at the annual Biophysical Society 56th Annual Meeting.

SUSAN MARQUSEE was awarded the 2012 William C. Rose Award from the American Society of Biochemistry and Molecular Biology (ASBMB). The William C. Rose Award recognizes outstanding contributions to biochemical and molecular biological research and a demonstrated commitment to the training of younger scientists. She was also selected as one of the Bay Areas 100 most influential women by the San Francisco Business Times. This is her second time receiving this honor.

CRAIG MILLER has been awarded the Regents' Junior Faculty Fellowship for Summer 2011 and is a recipient of the Hellman Family Faculty Fund.

DAVID H. RAULET was selected as Distinguished Lecturer for the 2012 Annual Conference of the American Association of Immunologists.

RANDY SCHEKMAN has been named the first editor of a journal by HHMI, the Max Planck Society, and the Wellcome Trust that will begin publication next year.

JEREMY THORNER was elected by the parent community at Berkeley High School (where his daughter is a Freshman) to serve as a representative on the school's BSEP Committee, which decides how to best spend the allotted funds raised by the "Berkeley Schools Excellence Project", a citizen-initiated tax measure, initiated in 1986 and re-approved by Berkeley voters in 1994, 2004, and most recently in 2006 for another 10-year period.

QING ZHONG was awarded an American Cancer Society research grant ($720,000 for four years), which targets junior faculties in their first six years.

MCB neurobiologist David Presti exchanges greetings with His Holiness the Dalai Lama at a meeting on "Cosmology and Consciousness" held in Dharamsala, India in December 2011. Over the last 25 years, the Dalai Lama has been the inspiration for a number of dialogues on topics generally believed to be among the great unanswered questions of contemporary science.

2010-2011 Graduates

Fall 2010

- **Colin Brown** (Eisen) The Evolution of a Transcription Factor: Divergence in DNA Binding Behavior of the Sex-Determination Gene hermaphrodite in the Genus *Drosophila*
- **Venice Calinisan** (Martin) Oct3 and Sox2 Expression in Mammary Carcinoma Cells
  Peter Cameron (Scott) The Molecular Basis for Water Taste in *Drosophila*
- **Susheela Carroll** (Drubin) Uptake of Toxin K28 and Early Endocytic Site Formation in *S. cerevisiae*
- **Jack Dunkle** (Cate) Structural Studies of the Elongation Cycle of Protein Synthesis and Its Inhibition by Antibiotics
- **Elif Nur Firat** (Welch) Dissecting the Mechanism of Arp2/3 Complex Activation by Actin Filament Binding and the Regulation and Function of JMY in Cells
- **James Fraser** (Alber) Beyond the Model and Into the Map: A Protein Abstract
- **Adam Freund** (Campisi) Signaling Pathways that Regulate Cellular Senescence
- **Phung Gip** (Bertozzi) Characterizing glycans on stem cells for discovery of biomarkers and biological significance
- **Roberta Hannibal** (Patel) Mesoderm Segmentation in the Amphipod Crustacean *Parhyale hawaiensis*
- **Nadine Jahchan** (Luo) Role of SnoN in Normal Epithelial Function and Tumorgenesis
- **Richard Lusk** (Eisen) Models to Mechanisms: Leveraging Functional and Evolutionary Information to Describe Regulatory Sequences
- **Deng Pan** (Luo) SnoN is a Stress Transducer that is Able to Function as a Tumor Suppressor *in Vivo* by Interacting with the PML-p53 Pathway
- **Andrea Pezda** (Coscoy) TLR9 Immune Evasion by Murine Gammaherpesvirus 68
- **Thomas Russell** (Werblin) Neuronal Circuitry of the Local Edge Detector Retinal Ganglion Cell
- **Yvette Soignier** (Martin) Oct3 and Sox2 Expression in Mammary Carcinoma Cells
- **Anna Wiedmann** (Komeili) The Role of Two HtrA/DegP Family Proteases, MamE and MamO, in Protein Sorting and Biomineralization in *Magnetospirillum magneticum* str AMB-1
- **Sarah Windler** (Bilder) Regulation of Cellular Signaling Pathways by Endocytosis and Protein Degradation

Spring 2011

- **Veronica Anania** (Coscoy) From Virology to Cell Biology, Understanding Unconventional Ubiquitination
- **Roman Barbalat** (Barton) Non-nucleic Acid Based Viral Recognition
- **Angela Brooks** (Brenner) RNA Splicing Regulation in *Drosophila melanogaster*
- **Meredith Carpenter** (Cande) Nuclear Inheritance and Genetic Exchange in *Giardia intestinalis*, a Divergent Eukaryote with Two Nuclei
- **Johanna Carroll** (Weis) Post-transcriptional Regulation of Gene Expression by the DExD/H-box Protein Dhh1
- **Shih-Chieh Chien** (Garriga) The Role of Wnt Signaling in *C. elegans* Neuronal Development
- **Jacqueline Chretien** (Dernburg) Characterization of Spermatogenesis in the Planarian *S. mediterranea*
- **Bryan Clarkson** (Doudna) Translational Control in Fungi
- **Mary Couvillion** (Collins) Piwi-bound Small RNAs in *Tetrahymena thermophila*
- **Ann Marie Faust** (Barnes) Regulation of Mitotic Progression in *Saccharomyces cerevisiae* by the Microtubule-associated Proteins Slk19 and Stu1
- **Malik Francis** (Rio) Identification and Characterization of the *Drosophila* Inverted Repeat Binding Complex
- **Yassi Hafezi** (Hariharan) Identification of Novel Regulators of Cell Competition in *Drosophila melanogaster*
- **Cathleen Haglund** (Welch) *Rickettsia* Sca2 is a Bacterial Formin-like Mediator of Actin-based Motility
- **Saori Haigo** (Bilder) Cellular and Molecular Mechanisms Underlying Tissue Elongation of the Developing Egg in *Drosophila melanogaster*
- **Hector Huang** (Groves) Studying Membrane Anchor Organization in Living Cell Membranes
- **Heiyoun Jung** (Raulet) Expression of Ligands for the NKG2D Activating Receptor are Linked to Proliferative Signals
- **Evguenia Klimenko** (Thorner) New Tools and Approaches for Studying the Role of the *Saccharomyces cerevisae* phosphatidylinositol 4-kinase Pik1 in the Yeast Nucleus
- **Laura Lombardi** (Rine) Maintenance of Open Chromatin States by Histone H3 Eviction and H2A.Z
- **Kathryn Monroe** (Vance) Type I Interferon is Not Just for Viruses: Cytosolic Sensing of Bacterial Nucleic Acids
- **Maria Mouchess** (Barton) Self/Non-self Discrimination by Toll-like Receptor 9
- **Jesse Patterson** (Thorner) Function and Signaling Specificity of the Hog1 Mitogen-Activated Protein Kinase in the Yeast *Saccharomyces cerevisiae*
- **Rebecca Pferdehirt** (Meyer) Targeting X Repression: Recruitment, Binding and Function of the *C. elegans* Dosage Compensation Complex
- **Alberto Stolfi** (Levine) Patterning of the *Ciona intestinalis* Motor Ganglion
- **Jeffrey Woodruff** (Barnes) Mechanisms of Mitotic Spindle Disassembly and Positioning in *Saccharomyces cerevisiae*
- **Veronica Zepeda** (Cate) Mechanisms and Regulation of Cellulose Degradation by *Clostridia papyrosolvens* C7 and *Neurospora crassa*
- **Rachel Zunder** (Rine) The Regulation of Chromatin Dynamics by Histone Chaperones and Variants

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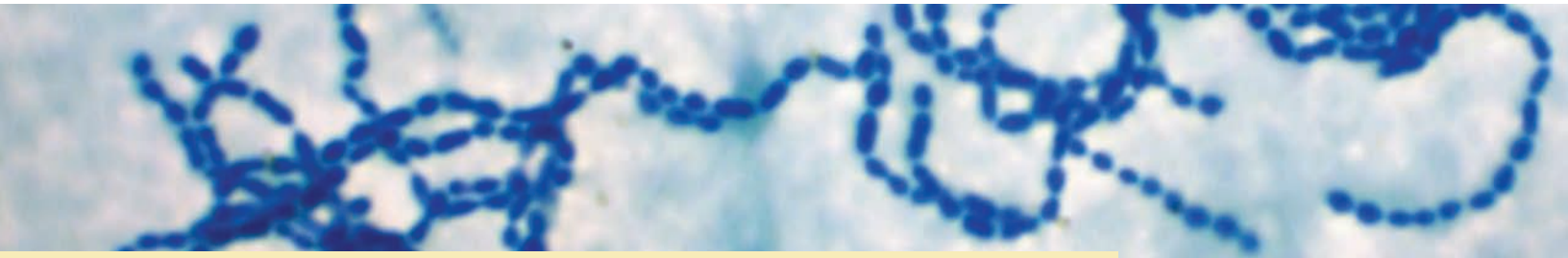
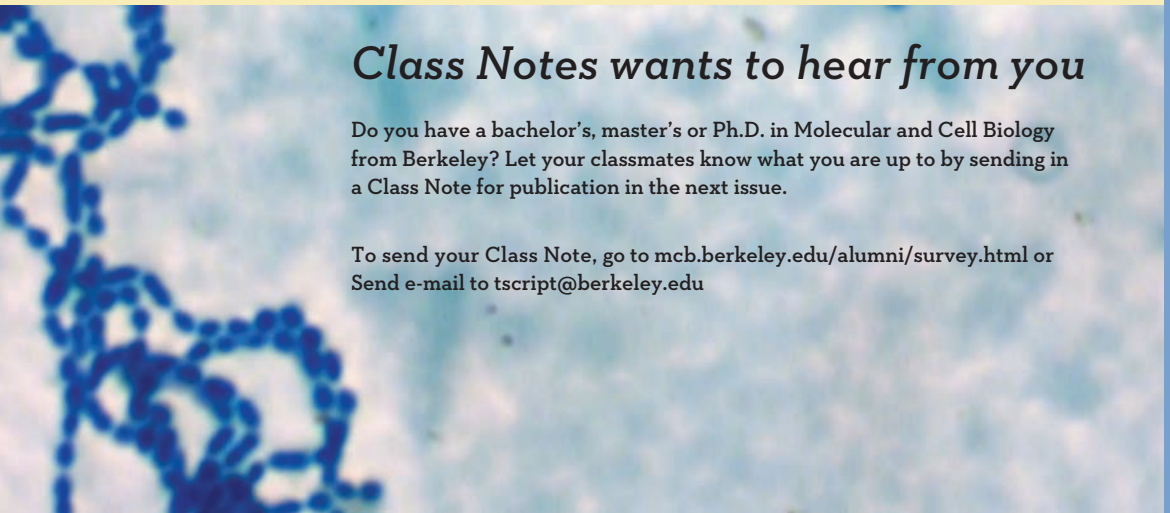


Class Notes

Christopher Julian [BA 1987] attended Georgetown Medical School in Washington, D.C. and graduated with honors. While remaining loyal to the Golden Bears, he completed his residency in Urology at Stanford University Hospital. He lives in Friant, California with his lovely wife of 16 years, Julie, and their daughter Eva, 15. He enjoys the balance between private practice, parenting, and the pursuit of packed powder or manicured fairways.

Rajiv Mahadevan [BA 1997] is the founder and President of Applied Immunology, which specializes in designing and implementing a variety of complex immunoassays to support the development of therapeutics, vaccines and diagnostics. The company is based in the bay area and serves customers around the world. He received an MBA from Stanford University and after that spent several years at Amgen, the genetics company 23andMe and has been a consultant/advisor to the Global Health division of the Bill & Melinda Gates Foundation. He lives in Palo Alto with his wife and two young girls. [rajiv@appliedimmunology.com]

Boback Ziaeian [BA 2002] happily married Sarah Mourra on June 6, 2008, finished a degree in Internal Medicine at Yale University June 2011, and is starting a fellowship in Cardiology at the UCLA STAR program in July 2012.



Class Notes wants to hear from you

Do you have a bachelor's, master's or Ph.D. 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, go to mcb.berkeley.edu/alumni/survey.html or Send e-mail to tscript@berkeley.edu

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