the Promoter

What's Going On In There:
Fluorescence Imaging at Carnegie Mellon University

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Spring 2013 No. 15 | Department of Biological Sciences at Carnegie Mellon University

From the Department Head

"What's new?" Many conversations begin with this phrase. In the Department of Biological Sciences the answer is typically "lots!"

The field of biological sciences is always **new** as technology and the focus of the field changes rapidly from year to year. As a department, we are constantly adapting to improve our teaching, training and research in ways that reflect the future of the field. Dr. Subra Suresh, the current National Science Foundation director and incoming Carnegie Mellon University president has stated that science is leaving the "Era of Observation" and entering the "Era of Data and Information." While interest in "Big Data" is exploding across all fields of science, I think that its potential impact in biology and medicine may be greater than in any other field. Historically most discoveries in biology came from combinations of careful observation, background knowledge and intuition, while the problems confronted by today's biologists benefit from and often require analysis of large data sets. A typical student now might need to analyze data from genomic, proteomic or imaging experiments either to make efficient progress in the lab, or to understand how some experimental result was obtained. At Carnegie Mellon, we want to make sure that our students are prepared for this future.

In recent years, we have adapted our curriculum to emphasize the importance of quantitative approaches in biological sciences. For example, we now require all biological sciences majors to take a course in computational biology. We believe that these changes are important in order to better prepare all students to succeed in biomedical fields in coming years.

Another **new** development causing much discussion throughout higher education is how online courses and innovative classroom technologies will influence the ways in which students learn. For many years, CMU's Open Learning Initiative (OLI) has been a pioneer in the development of feature-rich, interactive online courses that are based on a deep understanding of how students learn and the conceptual structure of the subject matter. The depth and care of CMU's efforts distinguishes it from the model of massive online open courses (MOOCs) being explored in other universities. Also, a hallmark of the education that our department provides is the importance placed on doing science, not just learning the results of science. Whether it's in an undergraduate lab course or through a research lab experience, many of our undergraduates find working in lab to be their most formative experience at CMU. We are trying to find ways to expand and improve this critical component of the education that we provide.

Hiring **new** faculty is one of the most important decisions the department makes. New faculty bring fresh ideas about research and education, along with excitement and energy to the department. They also represent the department's predictions about future exciting directions of the field of biological sciences. This fall, we welcomed three new faculty members, who collectively strengthen our department in critical areas of neuroscience, genomics and microbiology. These new faculty – profiled in this issue of The Promoter – are rapidly integrating themselves into the research and teaching missions of the department. Drs. Aryn Gittis and Sandy Kuhlman are both neuroscientists working on understanding the development and plasticity of neural circuits. Dr. Gittis is focused on understanding the circuitry that underlies movement disorders, whereas Dr. Kuhlman is interested in how inhibitory neurons regulate activity and plasticity in sensory systems. Dr. Luisa Hiller is a microbiologist studying the role of genomic diversity and genomic plasticity in bacterial infections. Collectively, these three new hires will play an important role in shaping the future of teaching and research in the department.

I hope that all of you – friends and alumni of the Department of Biological Sciences –have a chance to tell us what is **new** with you by keeping in touch. Whether its via an e-mail or a post to our Facebook page, we love getting updates about the impact our department and our students are making beyond CMU's campus.

Nathan Urban, Department Head

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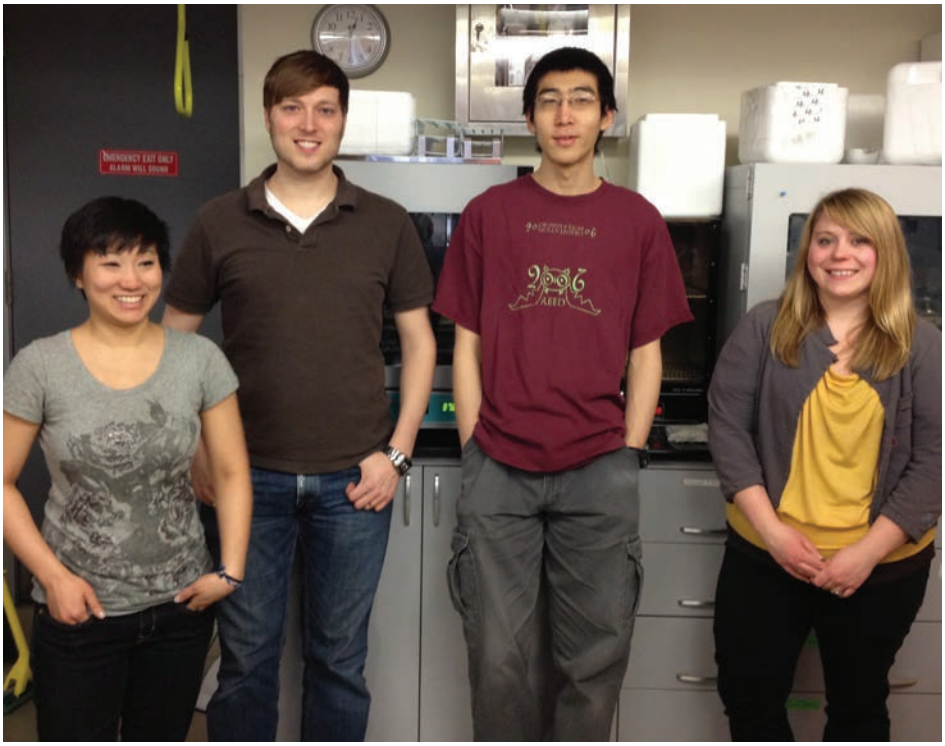
IMAGE & PHOTO CREDITS
Front Cover: Courtesy of the Murphy Laboratory. Page 3: Courtesy of The Sciences Teaching Club. Pages 4 - 7: Courtesy of the Laboratories cited under each photograph. Page 8: Courtesy of Ardon Shorr and PCR. Page 9: Kristen McConnell for the Department of Biological Sciences. Page 10 - 11: Alexander de Ronde for the Department of Biological Sciences. Page 12: Courtesy of Emerald Therapeutics. Page 15: Department of Biological Sciences. Back Cover: Carnegie Mellon University.

Future Faculty Explore Education Beyond the Bench

By Amanda Soohoo, Ph.D. Candidate



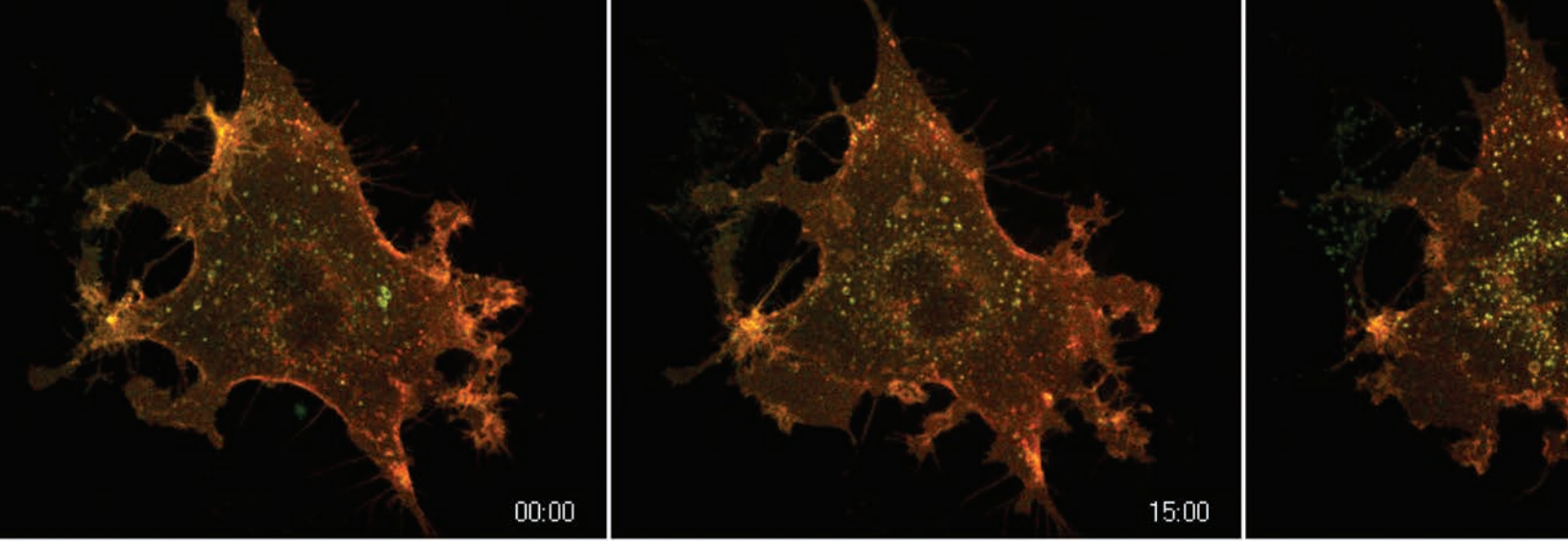
The Sciences Teaching Club Officer Board. Left to right: Amanda Soohoo, Andrew Kehr, Ming Zhang and Shanna Bowersox.

I am a terrible teacher. I talk too fast. I have no sense of timing for a lecture, and I cannot figure out how to contort my body in order to look at my students while writing on the board. I'm not a good teacher – not yet. The Sciences Teaching Club is helping me get there.

I didn't start graduate school knowing that I wanted to teach. The option was always there, the same way learning how to water-ski is always there, but I never really knew where to start. After all, teaching doesn't look too difficult; just stand up and talk. What most 20-something graduate students don't realize is that teaching is not natural. Effectively breaking down and communicating complex ideas to a room full of students is about as unnatural as getting a person to stand on water. Through my involvement with The Sciences Teaching Club, I am learning to stay afloat while teaching in graduate school instead of years down the road after I've fought pipette-tip and conical tube for a faculty position.

In the upcoming years, The Sciences Teaching Club plans to expand its reach beyond its current graduate student members from various science disciplines. The club particularly wants to become a resource about graduate education for undergraduates and complete outreach activities with non-science majors. In Fall 2013, the club plans to host a career panel on non-traditional academic careers and run a teaching portfolio workshop to prepare students for their job search. In a few weeks, Professor Dan Gurnon from DePauw University will be visiting with club members to speak about lecture design and his road to professorship. Dr. Gurnon's fluid and passionate nature instantly made him a teaching role model to club secretary Andrew Kehr.

If you have any questions regarding The Sciences Teaching Club, please contact Amanda Soohoo (asoohoo@andrew.cmu.edu) or Ming Zhang (mingruiz@andrew.cmu.edu).



Tracking endocytosis with a genetically encoded pH sensor. The β2-Adrenergic receptor is tagged with a unique genetically encoded reporter that binds to a cell-excluded pH sensor dye. This dye can then be used to track the receptor after drug-induced endocytosis, with color changes that correspond to local pH in endosomal compartments. Bruchez Lab.

What's Going On In There: Fluorescence Imaging at Carnegie Mellon University

By Marcel Bruchez, Ph.D.

Over the past 30 years, a brilliant program in biological imaging and microscopy has grown up at Carnegie Mellon University. Because digital imaging is so embedded into our daily lives, it's hard to believe that when imaging got started here in the 1990s, collecting a digital image from a microscope was a technical feat. But advances in imaging technology found fertile ground at CMU. Integrating probe development with automation and computational analysis helped transform the field of biological microscopy from an operator-dependent, visual scoring process to a high-throughput, quantitative and systematic approach to understanding the fundamental operations within living cells and organisms.

Imaging is integrated into almost any research program at CMU, but a number of researchers in Biological Sciences are developing and using new approaches in biological microscopy to improve the understanding of essential biological processes. The strengths of biological fluorescence are significant: subcellular resolution, multicolor detection, high sensitivity, and compatibility with living animals. Recent advances in fluorescent labeling developed at CMU allow direct observation of biological changes in cells and complex living organisms. Computational methods allow researchers to extract more information from simple imaging experiments, and improve the efficiency of comprehensive screening assays. These tools allow researchers to directly observe and understand how biological systems respond to their environments. Using the recently established and expanded shared imaging and biological automation facilities, CMU investigators continue to develop exciting research approaches using advanced biological imaging.

Bruchez Laboratory

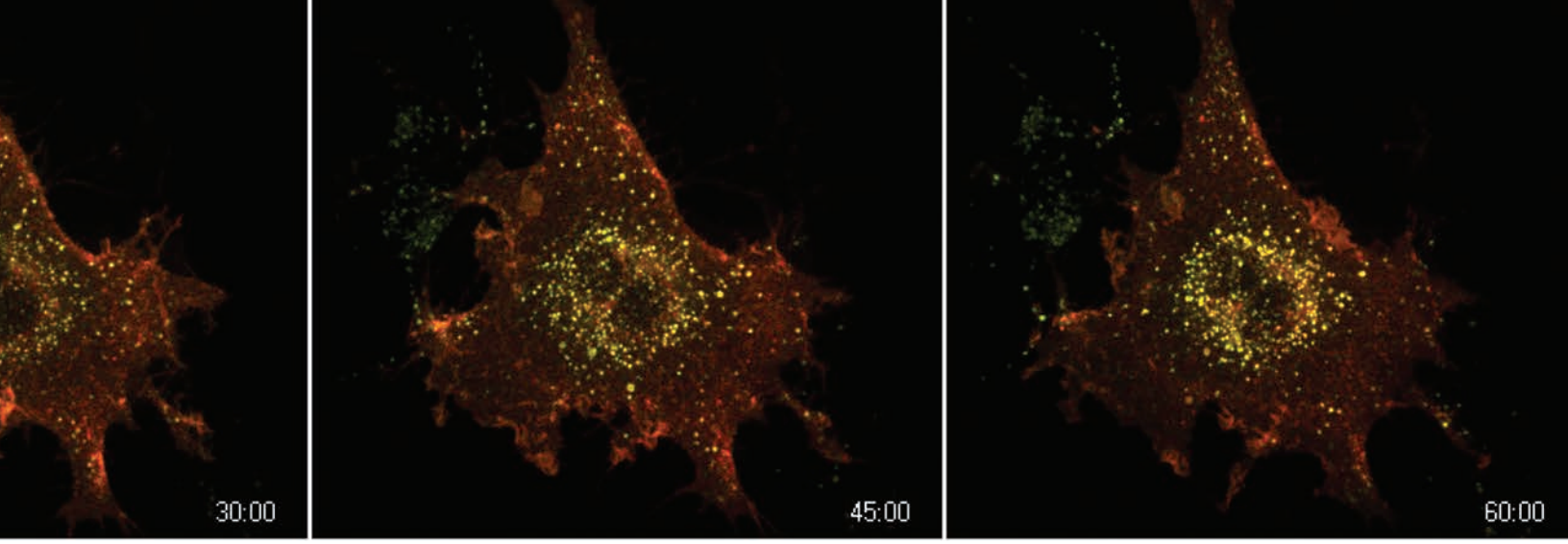
Proteins embedded in the plasma membrane regulate almost all communication between the cell and its environment. The fraction of protein at the surface, and the ability of the cell to readily mobilize or recycle internal reserves to the surface, play a role in basic processes like neurotransmission, glucose metabolism, and regulation of blood pressure. These processes are regulated differently in specialized cells and are highly dynamic in the cell, but they have been difficult to study using conventional encoded reporters. The Bruchez group has established a series of labeling tools that report on essential events in trafficking and recycling of surface proteins. Unique dye molecules can be targeted to expressed protein tags on living cells, activating fluorescence upon binding, and allowing detection of single molecules over many seconds. These probes can also carry sensitive environmental indicators, reporting on local changes in pH, reactive oxygen or Ca^{2+} concentration associated with the cellular response. These new probes are being applied in studies of synaptic vesicle recycling, ion channel surface expression and receptor signaling. The goal is to move from *in vitro* single cell studies to direct measurements of these trafficking properties in living animals, such as mice and zebrafish, allowing direct connections between *in vitro* cell biology and *in vivo* physiology.

Kuhlman Laboratory

The structure and function of the human brain is readily changed by life experiences, and these changes are most profound during so-called critical periods of childhood development. Why do the young seem to acquire new skills so effortlessly compared to adults? A research goal in the Kuhlman lab is to identify the specific biological circuit elements that initiate critical period learning in the young and are absent in adults. To accomplish this experimentally, functional responses of inhibitory neurons are measured *in vivo* using 2-photon guided electrophysiological recording of identified inhibitory neurons in anesthetized and awake mice.

Linstedt Laboratory

The Golgi complex is an intracellular organelle that processes proteins and lipids. The Golgi is divided into membrane compartments that are sequentially accessed much like a new car moving down an assembly line. It is difficult to assess the role cellular factors play in establishing these compartments, because the compartments

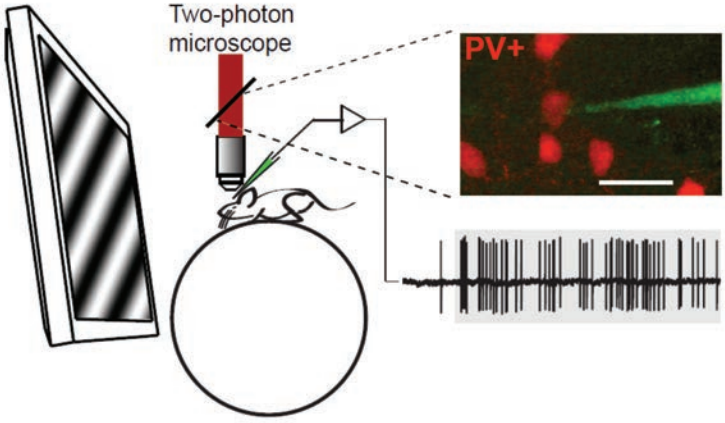


are separated from one another by mere nanometers and the flux through them is tremendous. To address this concern, Tim Jarvela, a graduate student working in the Linstedt group, has developed a strategy that uses light to inactivate a targeted cellular factor within seconds and tracks the consequences. For example, to test the hypothesis that the protein GRASP65 is specifically required for integrity of the first Golgi compartment, Jarvela used light to inactivate GRASP65. He then immediately used a fluorescence recovery assay to assess the integrity of the first and last Golgi compartments. The fluorescence coming from the first (red) and last (green) Golgi compartment was bleached in a small, boxed area. Recovery of fluorescence over time (shown in the boxes for each color and in the graph) indicates integrity of the compartment. As can be seen, the first compartment failed to recover while the last showed robust recovery indicating that GRASP65 is specifically involved in organizing the first Golgi compartment. Remarkably, inactivation of a related protein, GRASP55, gives the opposite result: disruption of the last but not the first Golgi compartment. Thus, these two proteins work in parallel reactions to maintain distinct compartments within a highly dynamic membrane system.

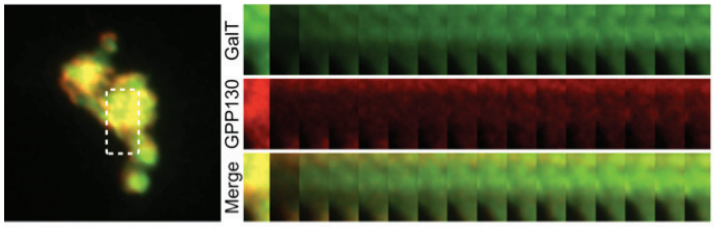
Minden Laboratory

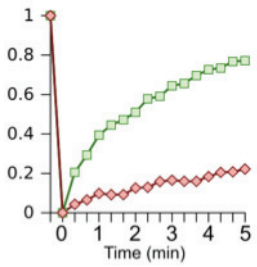
The Minden lab uses imaging in two very different ways, but with fluorescence at the core. First, they use fluorescence microscopy in conjunction with a variety of fluorescent probes to track several different cellular processes during the development of fruit fly embryos. In addition to the usual time-lapse recording of proteins tagged with Green Fluorescent Protein (GFP), a different reagent monitors where and when cells die and how their corpses get eaten to allow normal development to proceed. In collaboration with Stefan Zappe and Jelena Kovacevic in the Department of Biomedical Engineering, the Minden lab uses computer tracking software to follow this process, and determine if the detected patterns are normal or not.

The lab also uses fluorescence to analyze proteome differences between two samples, such as normal and cancerous cells. Using fluorescent dyes designed in collaboration with Alan Waggoner, Minden and his team can label the total protein from the two cell types with two different color fluorescent dyes. After labeling, the

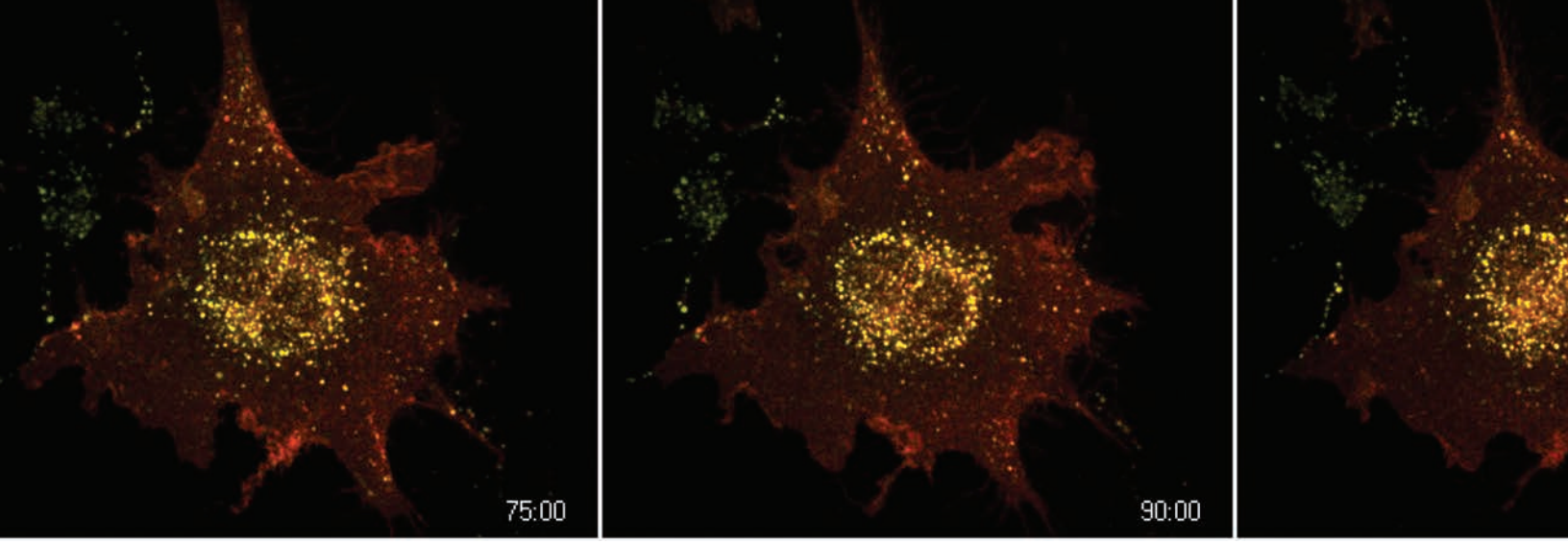


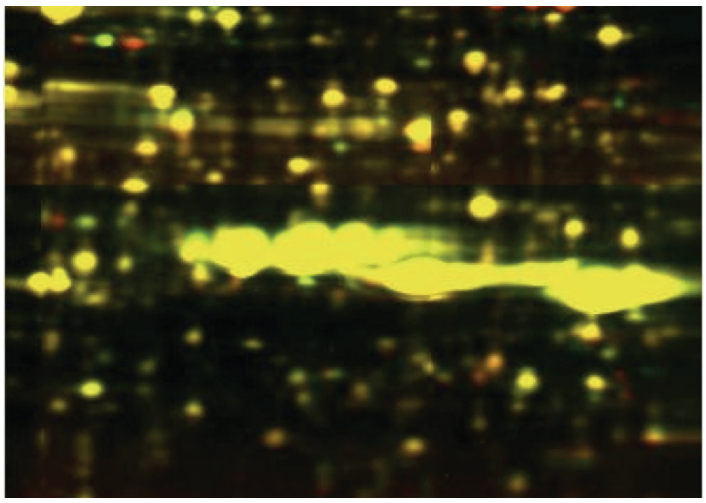
Imaging and recording neural activity in awake, behaving mice. Microscopy allows identification of inhibitory neurons (red), and targeted recording of electrical activity in an awake mouse on a spherical treadmill. Action potentials of an inhibitory neuron in response to a drifting grating visual stimulus are highlighted in gray. Kuhlman Lab.



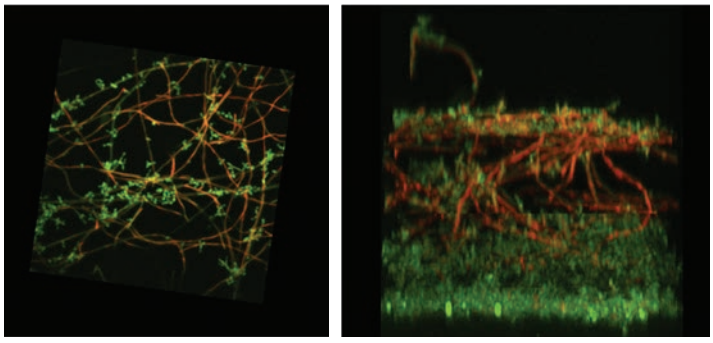


Light induced inactivation. The recovery of distinct cis and trans-Golgi compartment markers in a cell in response to GRASP65 inactivation using light indicates where this protein is involved in Golgi assembly and maintenance. Linstedt Lab.





Difference In-Gel Electrophoresis allows quantitative analysis of proteomic differences between two samples. Minden Lab.



***Candida albicans* biofilms imaged by confocal microscopy.** The left panel shows the yeast-form (rounded) and hyphal (elongated) cells visible by confocal fluorescence microscopy in a 17-plane axial projection near the apical surface of the biofilm, along with a sideview projection of the whole biofilm. Mitchell and Lanni Laboratories.

protein samples are mixed together and run on the same 2D electrophoresis gel. Then the gel is placed in a customized fluorescence imager that the Minden lab built, which allows them to capture fluorescent images of the gel using different wavelengths specific to the two fluorescent dyes used to label each sample. One of the technological hurdles Minden had to overcome involved the range of protein concentration. In the cell, protein concentration is several hundred thousand-fold, while the typical imaging system can only detect over a several thousand-fold range. To get over this barrier, the Minden lab used lessons learned from astrophysics and built an imager with a million-fold detection range, which allows for detection of most proteins in a cellular extract.

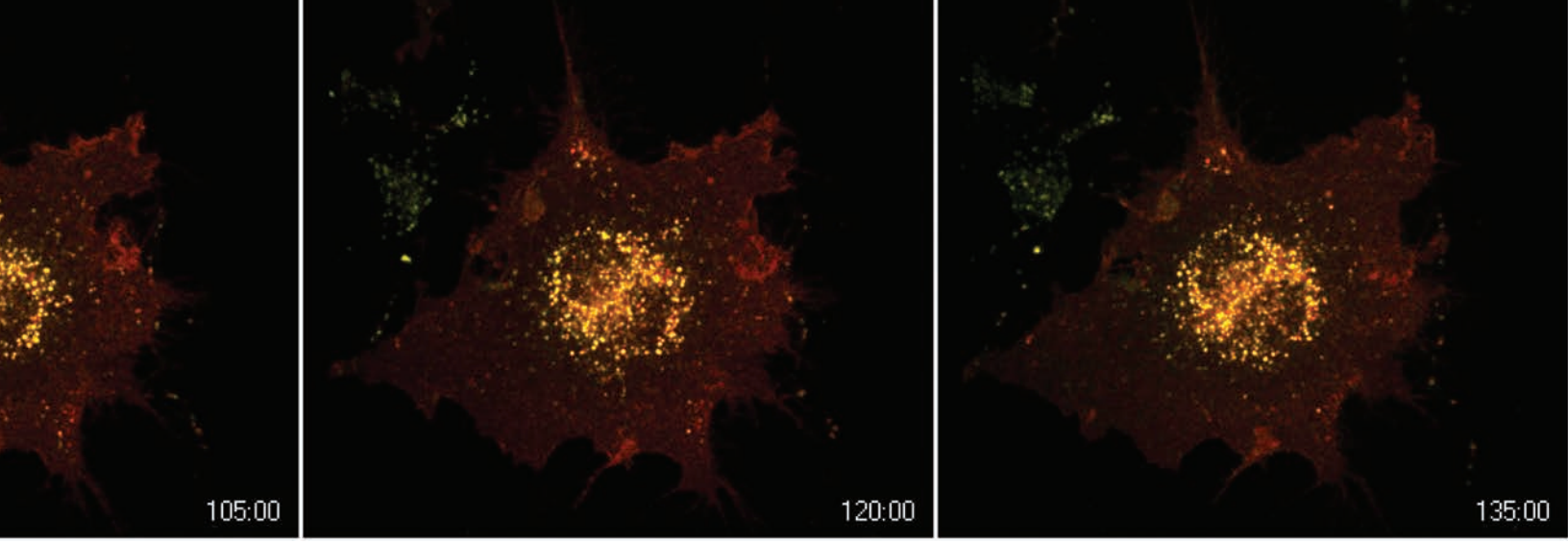
Mitchell and Lanni Laboratories

Invasive *Candida* infections cause over 10,000 deaths a year. These infections are difficult to treat because the fungus forms biofilms, surface-associated multicellular structures that are markedly different than free-living cells. The Mitchell and Lanni labs are using confocal fluorescence microscopy to study structure and function in biofilms of *Candida albicans*, a commensal fungus and opportunistic pathogen. Under usual conditions, biofilms are opaque due to the high refractive heterogeneity of *Candida* cells and hyphae. Mitchell and Lanni can alleviate this opacity using partial refractive index matching to enable light microscopy of fixed and living biofilms. They are able to use confocal microscopy to view cell structure through the thickness of a fully-developed biofilm.

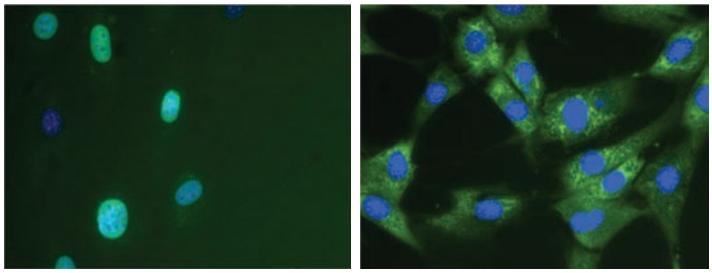
The research team imaged biofilms on a silicone elastomer at 12h, 24h, and 48h post-inoculation, using a red-fluorescent marker (RFP) when the cells are expressing genes associated with hyphal (filamentous) growth and a constitutive GFP marker. They found a rise in expression of the red reporter as a newly-inoculated biofilm develops over 48 hours. One of their immediate discoveries was that hyphal gene expression is not uniform, but strongest in the apical biofilm regions.

Murphy Laboratory

Where proteins localize in the cell and how localization is affected by potential drugs is an important element in the understanding of disease. Many diseases are associated with changes in protein localization and finding drugs that block those changes may provide new therapies. Significant advances in laboratory automation, such as



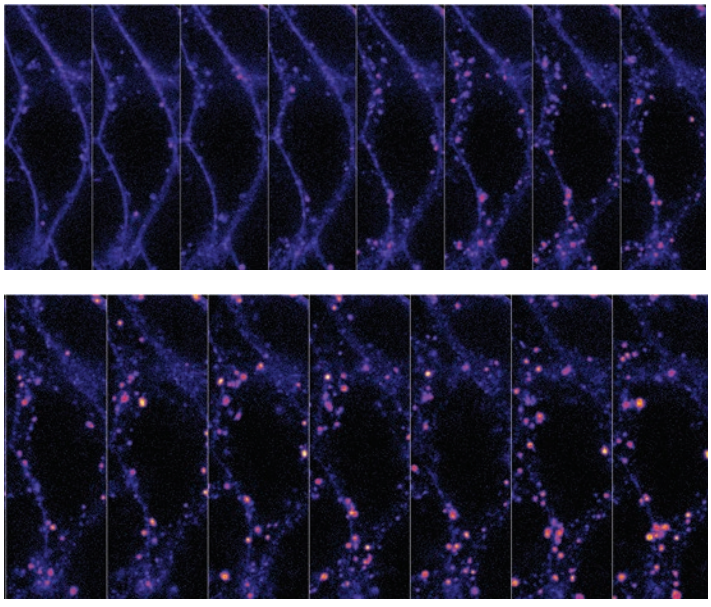
automated microscopy, liquid handling robots and robotic cell culture have enabled high-throughput screening of chemical compounds for desired effects. However, as there are roughly 10120 possible drug-like compounds and roughly 104 proteins in an organism, brute-force screening alone cannot teach us how all drugs affect all proteins. Therefore, what is needed is a combination of probabilistic models and an intelligent, machine-learning driven method of deciding what experiments are informative (in the sense of building more accurate models). The Murphy group has pioneered a method for intelligent screening in a data-driven fashion, and recently validated the method using liquid handling robots and an automated microscope. This equipment is in a new shared facility for laboratory automation in the Department of Biological Sciences. The method allows efficient learning of the response of many proteins to many drugs in living cells.



Automated microscopy of cellular responses to drugs. A dramatic change in the distribution of GFP-tagged PCK2 is seen in the presence (right) of calmidazolium. Murphy Lab.

Puthenveedu Laboratory

Drug addiction is a major worldwide socioeconomic problem. In the United States alone, about 10 percent of the population is addicted to illicit drugs. A large part of this population is addicted to opioid analgesics that form the mainstay of pain management in hospitals. Importantly, despite over 50 years of targeted efforts and billions of dollars spent on addressing this problem, neither a non-addictive opioid regimen nor a clear way to treat addiction exists. The principal hurdle in designing effective strategies against addiction is that we still do not fully understand the biological basis of why humans get addicted to some drugs. The wide range of opioid drugs that are clinically used and abused, such as morphine and heroin, activate the same targets that are activated normally in our brain by endogenous neurotransmitters. To truly solve addiction we need to understand why the receptors activated by neurotransmitters vs. abused drugs behave differently. One critical aspect of the normal physiology of these receptors is that they rapidly change their intracellular localization upon activation. The Puthenveedu lab has pioneered the use of high-resolution imaging assays, using novel receptor biosensors, to visualize drug-induced changes in receptor localization in living cells in real time. By extending these assays to sub-second temporal and single-event spatial resolution, they have identified potentially crucial differences in how receptors behave when they are activated by neurotransmitters versus drugs. The lab's current efforts are targeted towards understanding these differences at mechanistic and functional levels, with the goal of directing future efforts towards designing effective new methods to prevent addiction and relapse.



Receptors internalize after drug treatment. Confocal microscopy over time (20 s/panel) reveals redistribution of receptors into endosomes after drug treatment. Puthenveedu Lab.

What Researchers can Learn from Improv Theater

By Ardon Shorr, Ph.D. Student

Students explain their research at a PCR workshop.

Students listen to a lecture at a PCR event.

I'm sitting in the middle of a circle across from a graduate student, and we're trying to talk at the same time. We're not interrupting each other — I'm listening to every word, trying to repeat it back simultaneously. I shut my eyes but trail several words behind, never catching up.

The instructor stops us. "You're looking away, you've got to look at each other. Try it again."

She begins to speak, and we lock eyes. At some point I relax and fall into synchrony. I mirror her gestures, I'm attuned to every facial muscle, and the words flow through me as she says them. It looks like telepathy.

The instructor smiles. "Good. This looks like a silly game, but it has everything to do with science communication," she says. "When scientists talk about their work, we often put up a wall. We talk at someone. These theater techniques train us to open up, and reveal the person behind the science."

This workshop is part of *Public Communication for Researchers (PCR)*, a new initiative by three Ph.D. students in biological sciences, computer science, and machine learning. Their goal is for students to feel comfortable explaining their work and why it matters, whether to politicians, journalists, or grandmothers. PCR recruits speakers, runs mock interviews, and shares what they learn on their website.

And then there are theater games. I had no idea how they would help until we went around the room explaining what we work on. The stories were captivating. "I've known you for two years," said one student, "now I finally understand what you do!"

Departmental Highlights

Alison Barth (Faculty) received a 2013 Memory and Cognitive Disorders Award from the McKnight Endowment Fund for Neuroscience. She was also appointed to the Society for Neuroscience Program Committee, 2013-2015, which decides on the agenda, speakers, and topics for the annual Meeting of the Society for Neuroscience, the largest neuroscience society in the world.

Shanna Bowersox (Ph.D. '16) received the best poster award at the Center for the Neural Basis of Cognition annual retreat.

Simone Costa (B.S. '12) was named the 2012 recipient of the Elizabeth W. Jones Award for Excellence in Undergraduate Research. She was also awarded a National Science Foundation Graduate Research Fellowship.

Philip Davidson (Ph.D. '17) received the departmental 2012 Graduate Student Teaching Award.

Glen de Vries (B.S. '94) made a donation for the continuation of the de Vries Fellowship, an annual departmental award given to a graduate student in recognition of the impact and quality of a recent publication.

Dannie Durand (Faculty) was awarded a grant from the Human Frontiers Science Program for her work entitled "Evolutionary innovation in bacterial signal processing networks" with international collaborators Dr. John Pinney from Imperial College, London and Dr. Michael Laub from MIT.

Michael Gamalinda (Ph.D. '15) was awarded the 2012 de Vries Fellowship, a departmental award recognizing the impact and quality of a recent publication. He also received a travel fellowship from the RNA Society to present his work at the RNA 2013 Meeting in Davos, Switzerland.

Circle of Science: Developmental Stages of an Academic Career in Biology

By Ezgi Kunttas-Tatli, Ph.D. Candidate

Our scientific careers mimic embryogenesis — we develop over time. We start as a simple embryo, like a graduate student, and transform into a complex adult, like an academic professor. Similar to all organisms, we have to make sure that we possess the necessary components for successful development as well as avoid deleterious mutations along the way.

As the renowned developmental biologist Lewis Wolpert stated, "It is not birth, marriage, or death, but gastrulation, which is truly the most important time in your life." When this idea is applied to an academic career in biology, the last year of our Ph.D. becomes the most important time in our career. Prior to the last year, like a single-layered embryo, our time is spent in the lab conducting experiments, yet we are worry-free about grants and other responsibilities that our professors have. During our last year, we set up our three career layers like the three germ layers in gastrulation: publishing our Ph.D. work, finding a great post-doctoral position, and writing a grant. All of these layers have a major impact on our career.

Just as embryos don't rest after gastrulation in order to form all of the necessary organs during organogenesis, we must also be productive and improve all of the skills necessary to secure a faculty position during our postdoctoral years. Like organogenesis, we need to further specify and develop previously established career layers, which means more publications and writing in a shorter amount of time.

After we struggle as an embryo, finding a faculty position is like opening our eyes to the world for the first time. We have our own lab and it's time to grow. We need to learn how to balance our time between teaching, research, keeping up with meetings, and training new students. It is overwhelming, but like a little kid we are eager to learn and have the energy to do so.

When we finally reach adolescence, we are up for tenure! Like a teenager, we need to prove to everyone around us that we are a thriving independent researcher. We need to work hard to show our independence by publishing more papers with our name at the end of the author list.

Then, we enter the tenure years. We can now fully invest in our progeny: our graduate students. They will inherit everything from us for their own embryonic development. And the circle of life and science continues...

Aryn Gittis (Faculty) was named a finalist for The Eppendorf & Science Prize for Neurobiology.

Anmol Grover (Ph.D. '13) was awarded the 2012 Stupakoff Fellowship, a departmental award recognizing the impact and quality of a recent publication.

Stephanie Guerra (B.S. '12) was awarded a National Science Foundation Graduate Research Fellowship.

Veronica Hinman (Faculty) was awarded an Eberly Career Development Chair.

Chien Ho (Faculty) was named a fellow of the American Association for the Advancement of Science (AAAS). He also received a Gold Medal for his pioneering contribution of MRI-based cell tracking by the International Society for Magnetic Resonance in Medicine.

Karen Kormuth (Ph.D. '16) received the 2012 American Association of University Women Scholarship.

Ezgi Kunttas-Tatli (Ph.D. '14) received a Dr. Margaret Carver Biological Sciences Graduate Student Travel Award and Phi Kappa Phi Graduate Student Research Grant.

Jonathan Minden (Faculty) received The Richard Moore Award for substantial and sustained contributions to the educational mission of the Mellon College of Science. A book dedicated to the widely used difference gel electrophoresis (DIGE) technique, which was invented in the Minden lab, was published.

Aaron Mitchell (Faculty) was invited to serve on the advisory board for the Burroughs Wellcome Fund Investigators in the Pathogenesis of Infectious Disease Program. He also became chair-elect and lecturer for the American Society for Microbiology Division F, the Medical Mycology Division.

Departmental Highlights

Olivia Molinar (Ph.D. '16) received a Dr. Margaret Carver Biological Sciences Graduate Student Travel Award and GradUate Small Project Help (GUSH) funding from the Graduate Student Assembly (GSA)provost office.

Robert Murphy (Faculty) received the 2013 JBS Authors' Choice Award from the Society for Laboratory Automation and Screening for his paper entitled, "Automated Image Analysis for High Content Screening and Analysis." He was also featured in the special July 2012 bioimage informatics issue of *Nature Methods*.

Manojkumar Puthenveedu (Faculty) was awarded an Eberly Career Development Chair.

Eric Pederson (B.S. '15) and the rest of CMU's iGEM team earned the Best Foundational Advance prize at the International Genetically Engineered Machine (iGEM) Competition's World Championship Jamboree held in November in Cambridge, Mass.

Kiran Rafiq (Ph.D. '13) was awarded a Dr. Margaret Carver Biological Sciences Graduate Student Travel Award for the World Stem Cell Summit 2012 as well as GSA/Provost Conference Funding for 2012. She also received the Best Poster Award at the Developmental Biology of the Sea Urchin Meeting XXI for her poster entitled "Expanding the PMC GRN: Genome-Wide Analysis of Ets1 and Alx1 Targets."

Elizabeth Ransey (Ph.D. '16) received a UNCF/Merck Science Initiative Graduate Research Fellowship. She also secured a MARC Graduate Travel Award to attend the American Society for Biochemistry and Molecular Biology Experimental Biology Conference in Boston.

Abigail Simmons (B.S. '13) was awarded an undergraduate research fellowship from the American Society for Microbiology (ASM).

Ardon Shorr (Ph.D. '17) received a Graduate Research Fellowship from the National Science Foundation.

Jason Talkish (Ph.D. '13) received the Nomura Poster Award at the 9th International Conference on Ribosome Synthesis in Banff, Canada for his poster presentation entitled "The DEAD-box protein Drs1 physically interacts with Nop7 sub complex and is required for early steps of 27s of pre-rRNA Processing."

Rachel Vistein (Ph.D. '15) received the departmental 2012 Graduate Student Service Award.

John Woolford (Faculty) became a member of the advisory board for the Charles E. Kaufman Foundation.

New Assistant Professor
Aryn Gittis, Ph.D.

Postdoctoral Appointment, Gladstone Institute of Neurological Disease

Ph.D. in Neuroscience, University of California, San Diego

I study the organization and function of neural circuits in the basal ganglia, a primary motor control system in the brain. In particular, I am interested in how neurons in the basal ganglia wire together to create circuits and how these circuits are changed by experience and in movement disorders such as Parkinson's disease and dystonia. Developing a better understanding of how neural circuits are organized in the basal ganglia brings us closer to the ability to develop better treatments for a broad spectrum of human diseases.

My lab completes this research in mice because specific neural circuits for electrophysiological analysis and direct activation can be genetically labeled.

It is also an exciting time for basal ganglia research. In the last 10 years, new tools have been developed that enable an unprecedented ability to target and manipulate neural circuits in living animals. These tools are especially powerful in the basal ganglia, where neurons with very different functions are all intermingled with each other. Now, we have the ability to turn these different cell types on and off with high precision, enabling direct analysis of how complex neural circuits in the basal ganglia regulate behavior.

Over the next 20 years, I predict we'll see even more novel techniques to specifically manipulate neural circuits. It is my hope that we can translate these advances in basic research into new strategies to repair basal ganglia function in a variety of human diseases.

To further my research, I am collaborating with Dr. Alison Barth's lab. We would like to understand how sensory information affects the function of the basal ganglia, which is typically thought of as a motor circuit. I am also excited about the possibility of collaborating with computer scientists or mathematicians to develop more useful computer models of basal ganglia function.

New Assistant Professor
N. Luisa Hiller, Ph.D.

Postdoctoral Appointment, Center for Genomic Sciences, Allegheny-Singer Research Institute

Ph.D. in Immunology and Microbial Pathogenesis, Northwestern University Medical School

If you think you have done it all on your own, think again! Your body has ten times more bacterial cells than human ones. Many bacteria work to keep you in good health; however, there are also many bacteria that you do not want to meet in a dark alley. What mechanisms determine if they are friend or foe?

Over the past decade, our knowledge of bacteria has increased dramatically. They are responsible for both acute and chronic infections. They can organize into complex structured communities (biofilms), where they communicate and coordinate across cells. Different strains from the same species can have very diverse genomes; and new strains can be generated in the course of a single infection. Different bacterial genotypes and behaviors partially explain how bacteria from the same species can be either beneficial or harmful.

To investigate the diversity and plasticity of bacterial genomes, I study the bacteria *Streptococcus pneumonia*, which is associated with both acute (meningitis and pneumonia) and chronic disease (ear infections). My goals are to characterize genomic variability within bacterial populations, capture strain evolution during single infections and epidemics, and ultimately correlate individual genes and pathways to the molecular behavior of microbes and their hosts.

My current work addresses the evolution of *S. pneumoniae* in the post-antibiotic era by analyzing the whole genome sequence of strains isolated over the past century. My group also studies virulence and niche adaptation by identifying and characterizing signal transduction systems used to sense and respond to the surrounding environment. I hope that these studies on the evolution, fitness, and virulence of *S. pneumoniae* will provide a better understanding of the role of bacteria in human health and disease.

New Assistant Professor
Sandra Kuhlman, Ph.D.

Postdoctoral Appointments, University of California, Los Angeles (UCLA) & Cold Spring Harbor Laboratory

Ph.D. in Physiology, University of Kentucky

When faced with a new challenge, humans can achieve expert performance through practice. My research goal is to understand how neural networks in the cortex are altered during new skill acquisition to promote appropriate behavioral responses and to understand how the circuitry for learning is established during development. By understanding how microcircuits are altered during learning, we hope to be able to rescue learning deficits at the molecular and/or genetic insult level to restore circuit function.

My laboratory will visualize and track circuit changes in mice as they learn new skills through multiphoton laser-scanning microscopy as well as splicing jellyfish and coral DNA that codes for fluorescent protein into the genome of mice.

I currently collaborate with a vision lab at UCLA and a lab at UC Irvine specializing in a 'laser scanning photostimulation' technique. This technique quantifies strengths of connections among neurons within a local microcircuit. Our team has discovered that manipulation of visual experience very rapidly alters how inhibitory circuits are recruited in the brain, and that this appears to be required for adaptation to the new condition. I also work with a lab at The Johns Hopkins University training mice to discriminate the position of a small object, and imaging the cortex as the mouse becomes an expert at localizing the object. We find a significant change in the connections between sensory and motor brain areas. This change actually precedes improved performance, so it may be a predictor of future expertise.

In the future, I hope to collaborate with David Lewis's lab at the University of Pittsburgh. We have a common interest in molecular signaling pathways, which are required for inhibitory neurons to wire up into cortical circuits. I also look forward to interacting with Carnegie Mellon engineers, such as Shawn Kelly, to develop sophisticated brain activity monitors so biofeedback may be used to accelerate learning and perhaps rescue learning deficits.

Alumni Profile: D.J. Kleinbaum's Journey to Co-founding Emerald Therapeutics

By Mridula Nadamuni, Senior

The Emerald Therapeutics Team. Row 1: Alex Yoshikawa (CIT '12). Row 2: Courtney Webster, Catherine Hofler (MCS '05), DJ Kleinbaum (MCS '05). Row 3: Brad Bond, Ruben Valas (SCS '05). Row 4: Jonathan Leung (CIT '11), Robert Teed, Brian Frezza (MCS '05), Benjamin Kline.

Wanted: Passionate, creative-thinking problem-solvers interested in disrupting the traditional landscape of biotechnology.

Emerald Therapeutics is doing just that. Co-founded by alumni D.J. Kleinbaum and Brian Frezza, the company is taking an interdisciplinary approach to solving the problem of persistent viral infections that the body cannot clear on its own. The three-year old Silicon Valley startup is looking to revolutionize the biotechnology industry. Kleinbaum credits much of Emerald Therapeutics's early success to the time he spent as a biological sciences student at Carnegie Mellon University.

In Fall 2001, Kleinbaum began his undergraduate studies within CMU's Department of Biological Sciences by enrolling in the innovative and rigorous computational biology program. His high school friend Frezza enrolled as well. The computational biology major prepares students to use computer science principles to explore biology. However, as his studies progressed, Kleinbaum found himself moving away from programming and devoting more time to biological sciences and chemistry.

In order to find his true interests and gain hands-on experience, he also worked in Dr. Bill Brown's laboratory engineering antibodies to act as environmentally sensitive fluorescent biosensors. He created a program to analyze 3D protein structures and identify candidate residues to which fluorophores could be covalently attached. Next, he spent months on bioconjugation experiments to test his predictions. Kleinbaum says "He [Brown] was an amazing mentor, and part of the fact that the research followed my interests was that he could see my interests changing. He was willing to let me follow the parts of

Alumni Updates

Sarah Ackermann (B.S. '11) works for Dr. Scott Lowe as a research technician/lab manager at Memorial Sloan-Kettering Cancer Center.

Susan Alfs (B.S. '10) finished her Master of Bioscience at Keck Graduate Institute of Applied Life Sciences (Claremont Colleges, Calif.) in May 2012. She is now a validation associate II at Baxter Bioscience in Thousand Oaks, Calif.

Elizabeth (Wickert) Allard (B.S. '89), received an M.D./Ph.D. degree from Brown University and is a family practitioner at New London Family Practice in New London, Conn. She is married to Gregory (CIT '88); they have two sons.

Tabitha (Sotomayor) Ames (B.S. '05) founded Luminary Birth Services. In Jan. 2012, she also joined the Childbirth and Postpartum Professional Association's faculty as California's childbirth educator trainer. She lives in the San Francisco area with her husband, Jon (CIT '04), and their daughters Juniper and Niobe.

Tom Anfuso (B.S. '91) is the vice president of Enterprise and Infrastructure Business Systems at USAA in San Antonio, Texas. He and his wife have two children.

James Araujo (B.S. '05) is completing the first year of his clinical gastroenterology fellowship at Columbia University and plans to spend the next two years focusing on esophageal cancer and Barrett's esophagus.

Jeya Balaji Balasubramanian (M.S. '10) is a data analyst and research programmer at the Department of Biomedical Informatics, University of Pittsburgh.

the project that I was the most passionate about, which was hugely valuable." There is no doubt in Kleinbaum's mind that undergraduate research taught him to troubleshoot—a skill Emerald values immensely. Kleinbaum graduated from CMU in 2005 with a B.S. in Biological Sciences and chemistry minor.

Though he was anxious to enter the biotechnology industry following graduation, a Ph.D. was considered essential at the time so Kleinbaum joined a chemistry lab at Stanford University for further education. Meanwhile, Kleinbaum remained in close contact with Frezza, who also moved west to join The Scripps Research Institute. The pair soon returned to their dream of opening a lab—it was just a matter of waiting for the right time.

The right time proved to be following their doctoral graduations in 2010; they began in earnest only to find that a biology-based start-up is an expensive venture. Kleinbaum and Frezza found themselves in a catch-22 situation: wooing investors and purchasing equipment required preliminary results, which they couldn't provide without a lab.

Luckily, CMU came to rescue. With the help of Biological Sciences Professor John Woolford, Kleinbaum and Frezza prepared to sign an agreement with CMU to run Emerald Therapeutics out of the Mellon Institute. In May 2010, Kleinbaum and Frezza sold their furniture, packed up their cars, and mapped out the route to Pittsburgh.

But, life is full of surprises. On the same day that they planned to leave, Kleinbaum received an invitation to a meeting with a venture capital firm. Still intending to hit the road that night, the two dug out their suits from boxes. After the meeting, the investor convinced the pair to remain in Palo Alto for another week. The week became a month as the pair continued to generate interest among investors. When investor and PayPal co-founder Peter Thiel came on board, they knew that there was no going back. Emerald Therapeutics officially opened in September 2010 in Menlo Park, Calif.

In addition to working with viral infections, Emerald Therapeutics is interested in bringing process automation and robotics to mainstream scientific research. The company developed an internal product, "Symbolic Lab Language (SLL)," out of a need to maximize the effectiveness of their lean workforce. SLL, layered on top of the Mathematica programming language, standardizes protocols, controls instrumentation, parses experimental outputs, and presents and analyzes data. This allows Emerald's scientists and engineers to control a large number of accurate and reproducible experiments at once.

"At CMU, there's no fear of crossing disciplines, and that is [Emerald Therapeutics] most valuable asset."

D.J. Kleinbaum

Kleinbaum encourages students interested in entrepreneurship to get early exposure to industry. He admits that Emerald Therapeutics preferentially seeks CMU students. "At CMU," he says "there's no fear of crossing disciplines, and that is our most valuable asset."

Nancy Grasmick Barnard (B.S. '58) retired from the Department of Zoology at Vassar College and the director of a bacteriology laboratory at an EPA-certified environmental lab. She now takes part in the Academy of Life Long Learning at Western Washington University.

Kristina Behan (Ph.D. '01) was promoted to professor at the University of West Florida. She is also the program director for the Clinical Laboratory Sciences.

Candace (Spier) Bever (B.S. '04) is a postdoctoral scholar at the University of California, Davis in the laboratory of Dr. Bruce Hammock researching environmental and human health monitoring. Concurrently, she was promoted to research translation coordinator for the UC Davis Superfund Research Program. She earned a Ph.D. in Marine Science from the College of William & Mary in 2011 and participated in the AmeriCorps National Civilian Community Corps program from 2004-2005.

Anish Bhaswanth (M.S. '11) is a systems level programmer (bioinformatics analyst) in Dr. Uma Chandran's laboratory at the University of Pittsburgh.

Charlene (Mason) Brisbane (B.S. '88) is the manager of biopharmaceutical technologies at GlaxoSmithKline in King of Prussia, Pa. She resides in Horsham, Pa. with her daughter, Shelby.

Dara Brown (M.S. '08) received a veterinary medicine degree from the University of Pennsylvania in 2012. She is now completing an equine internship in Charlottesville, Va.

Lilyanne Chen (B.S. '10) is a first-year student at Tulane University School of Medicine.

Alumni Updates

Jessica Chu (B.S. '04) and her husband, Justin, were married in January 2013.

Katherine Cummings (B.S. '07) finished veterinary school at Michigan State University as well as an internship at Michigan Veterinary Specialists. She is now in the first year of an anesthesiology residency at Tufts University.

Marciela DeGrace (B.A. '07) married Ioan "Teo" Ifrim (DC, '07) in April 2012. She also finished her Ph.D. in virology from Harvard University. Her thesis was entitled "RNAi screens in primary human lung cells reveal Hermansky-Pudlak Syndrome proteins as influenza suppressors." She is now a Presidential Management Fellow at the National Institute for Allergy and Infectious Disease, National Institutes of Health.

Joseph DeMasi (B.S. '95) was promoted to associate professor of biology at the Massachusetts College of Pharmacy and Health Sciences in Boston. He also serves as the premed advisor and program director for the biology major.

Beverly Deerhake (B.S. '62) and her husband traveled to Bulgaria to learn about the Roma, bringing their traveling total to 111 countries. She will be teaching about her experience with the Roma over the next year.

Molly Evans (B.S. '11) was awarded a National Science Foundation Graduate Research Fellowship.

Rebecca Frederick (B.S. '01), after an American Cancer Society postdoctoral fellowship at the Carnegie Institution for Science in Baltimore, is now an American Association for the Advancement of Science (AAAS) Science and Technology Policy Fellow in the Office of Science Policy and Planning at the National Institute of Neurological Disorders and Stroke, National Institutes of Health in Bethesda, Md.

Rachel (Dub) Friedman (B.S. '03) graduated from the Emergency Medicine Residency Program at Allegheny General Hospital and began her career as an emergency medicine physician at Allegheny Valley Hospital. Her family, including husband, Alex and stepdaughter, Josie, welcomed a son, Benjamin, in 2012. They reside in Pittsburgh.

Joy Fuchs (M.A. '70) continues to enjoy teaching hands-on science to preschoolers in the metro Atlanta area as part of Science Excitement, Inc.

Brooke Goldner (B.S. '99) developed the online psychiatric practice, SkypePsychiatrist.com, where she works with individuals across California. She also gives lectures on healing physical and mental illness using natural foods. Her family recently welcomed another son.

Elena Hawryluk (B.S. '01) is the chief resident of dermatology at Harvard Dermatology in Boston, Mass.

David Hill (B.S. '05) will be graduating from the M.D./Ph.D. program at the University of Pennsylvania Perelman School of Medicine and starting a residency in pediatrics in July. He and his wife, Joanna, welcomed a daughter, Elia, in September 2012.

Jason Kang (B.S. '90), after completing a Ph.D. from Thomas Jefferson University, postdoctoral appointments at Stanford University and the National Institutes of Health, living in Korea to work for sequencing service provider, Macrogen, Inc., and living in Singapore to work for Applied Biosystems (now Life Technologies), is now back in the United States working as the district sales manager mid-atlantic for Life Technologies. He resides in the Philadelphia area with his wife, Gina, and two sons.

Sharon Kardia (B.S. '85) is the senior associate dean of the School of Public Health at the University of Michigan in addition to her regular professorial duties and research into the human genetics of common diseases.

Deborah Keller (B.S.A. '99) is finishing a colorectal surgery fellowship at University Hospitals Case Medical Center in Cleveland. She will begin working in the Department of Colon and Rectal Surgery at Penn State Hershey in July.

Cheng-Neng (Mark) Ko (M.S. '09) is a senior financial software developer at Bloomberg LP.

Yutong Li (M.S. '12) is a quality engineer at Microstrategy Inc.

Mark Licata (B.S. '82) is the co-founder of Intelliject.

Lindsay Liu (B.S. '09) is the director of global marketing at Method, a design firm creating digital products and services. Two of her recipes will be published in the book,"Ultimate Nachos," in April 2013.

Elyse Maiorini (B.S. '08) will graduate in May 2013 and receive a DMD from the Harvard School of Dental Medicine. Starting July 1, she'll be attending a general practice residency at the Carolinas Medical Center in Charlotte, N.C.

Bradley Malin (B.S. '00) was promoted at Vanderbilt University to an associate professor with tenure of biomedical informatics in the School of Medicine, associate professor of computer science in the School of Engineering, and vice chair for research in the Department of Biomedical Informatics.

Mia Markey (B.S. '98) edited a book on "Physics of Mammographic Imaging" which was published by Taylor & Francis in November 2012.

Diane McKay (B.S. '84) was recently appointed director of the graduate certificate programs at the Tufts University Friedman School of Nutrition Science and Policy.

Tamar Melman (B.S. '10) began a Ph.D. in computational biology at Cornell University in August 2012 after she biked from Boston to San Francisco during the summer.

Susan Montenegro (B.S. '06) left her position as a clinical pharmacist and started as a drug use analyst at the Food and Drug Administration.

Donna MacDougald Mott (B.S. '77) is moving to a lake house in upstate New York after spending the past 35 years as a research chemist with six patents, a mother to three sons, a U.S. patent agent and most recently a clinical pharmacist at Yale New Haven Hospital.

Carl Munson (B.S. '71)'s youngest son joined his father, mother, and brother as a Tartan, when he enrolled in CMU's computer science program this fall.

Marc Newman (B.S. '71) works for the Department of Veterans Affairs, Office of Information Technology helping to develop

and enhance the measures and metrics program. He is now a fellow in the Health Information Management Systems Society (HIMSS). He also welcomed a new grandchild this year, Jessica Alana.

Kimberly Parks (B.S. '08) will be graduating from Baylor College of Medicine in Houston with an M.D. and starting a residency in psychiatry.

Justine Record (B.S. '12) is a school-based health center AmeriCorps navigator with Open Door Family Medical Centers in Port Chester, N.Y. She is responsible for health education and outreach at JFK Magnet School.

Joana Ricou (B.S.A. '04) held her first solo show in Lisbon, Portugal at EdgeArts entitled "One, No One and One Hundred Thousand," which explored the biology of memory. In 2012, she received a Spark grant from the Sprout Fund to complete a science-art project about evolution at the Children's Museum of Pittsburgh and was a fellow at the STUDIO for Creative Inquiry.

Ashraf Saleemuddin (B.S. '03) is a second-year gastroenterology fellow at Boston University Medical Center.

Judy Savitskaya (B.S. '12) is a Churchill Scholar studying synthetic biology at Cambridge University.

Jeffery Schloss (Ph.D. '79) was recently appointed the director of the Division of Genome Sciences at the National Human Genome Research Institute, National Institutes of Health.

Judith Levenstien Schneider (B.S. '60) has her own private practice working with special needs children. Prior to opening her practice, she worked as a teacher and later as an assistant director at a school for children with disabilities.

Nina Senutovich (Ph.D. '11) is a post-doctoral associate in Dr. Lansing Taylor's laboratory at the University of Pittsburgh's Drug Discovery Institute, developing a human 3D liver model microfluidic device for improved pharmaceutical drug toxicity studies, drug discovery and investigation of human diseases. In 2012, she performed research in Chile's Atacama Desert to identify and determine the extent of microbial life in the arid desert environment with a NASA-ASTEP team.

Victoria Spindel (B.S.A. '08) is a dental student at Tufts University.

Leigh Stuckhardt (B.S. '07) is a health insurance specialist at the Center for Medicare and Medicare Services' Office of Legislation in Washington, D.C.

Marci Swede (Ph.D. '94) is an associate professor and chair of the Department of Health Sciences at Long Island University, CW Post, studying an anti fungal resistance pathway in *S. cerevisiae*. She lives in N.Y. with her husband, **Bruce Taillon (Ph.D. '94)**, and their two children, Aaron and Katy.

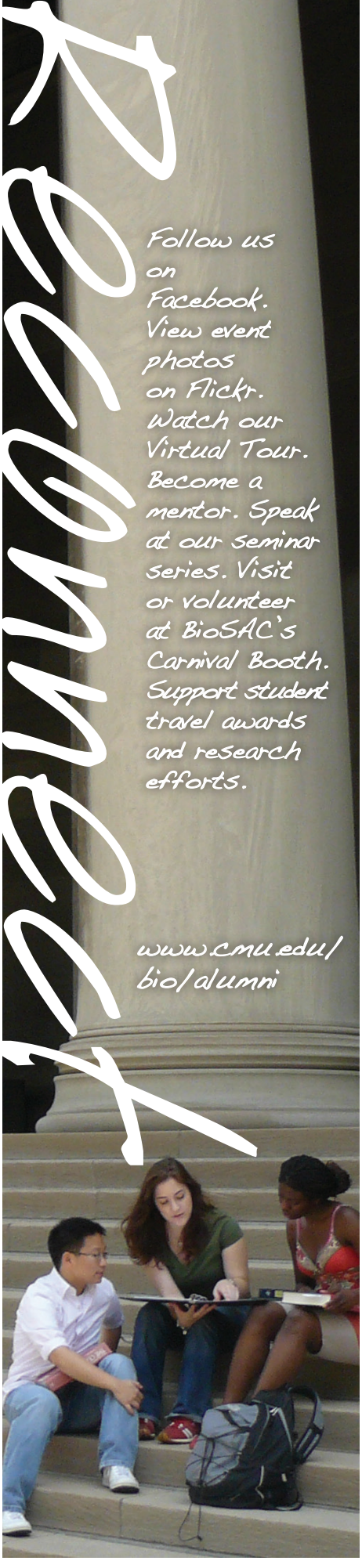
Daniel Warthen (B.S. '04) earned a Ph.D. in biology from the University of Virginia in August 2012, working in Dr. Iggy Provencio's lab. He is now a postdoctoral fellow in Dr. Michael Scott's lab in the Department of Pharmacology at the University of Virginia, studying the neurobiology of food consumption and obesity.

Jared Wenger (B.S. '06) and his wife, Jesse, welcomed a son, Fritz, on Dec. 26, 2012, joining brother, Freddy. Wenger works at Amyris, Inc. as a scientist developing yeast strains capable of producing renewable diesel fuel from cellulosic biomass sources.

Jessica Williams (B.S. '10) finished the post baccalaureate program at the University of Pennsylvania in 2012. She is now working at United Allergy Services, which provides allergy testing and immunotherapy to patients in a private medical practice. She also works at the Translational Core Laboratory at the University of Pennsylvania on the Renal Insufficiency Cohort Study.

Margaret Young (B.S. '05) is graduating from the Medical Scientist Training Program at Washington University in May 2013 with an M.D./Ph.D. in immunology. Her Ph.D. research was completed in the laboratory of Dr. Timothy Ley and her thesis was entitled "Genetics and Epigenetics of *in vivo* and *in vitro* Reprogramming." She starts a residency in pediatrics this summer.

David Zaidins (B.S. '12) is a research specialist at the University of Pittsburgh's Drug Discovery Institute.



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