Neuroscience News

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MacArthur Genius

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Message from Chris Evans, Director of the Brain Research Institute

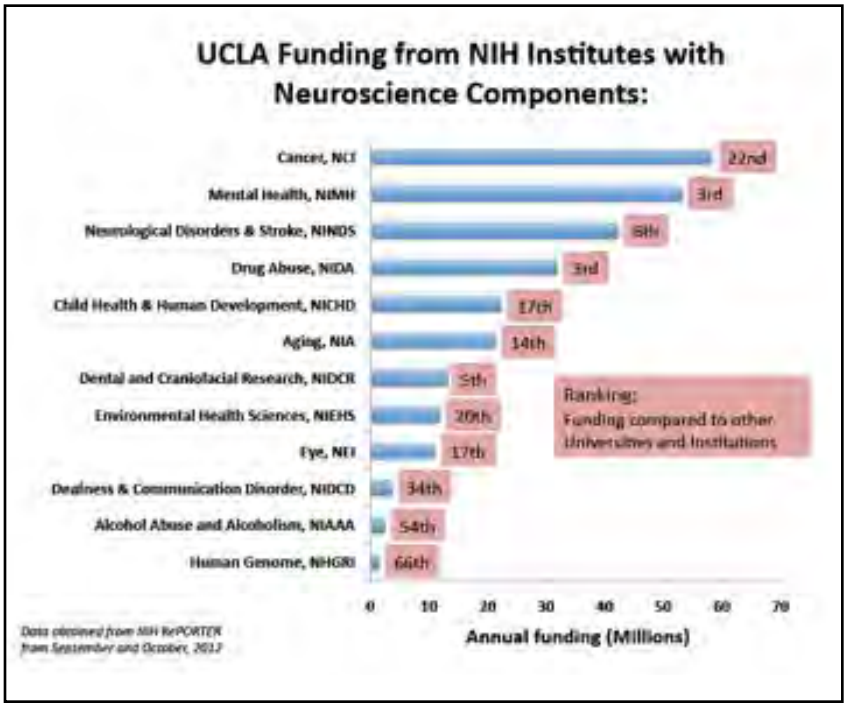
Dr. Chris Evans

This is the time of year when I usually focus on the significant accomplishments of the UCLA Brain Research Institute during the past 12 months. As usual, in 2012 our faculty, researchers and students have achieved enormous strides forward on the road to developing the basic science and clinical interventions necessary to eventually mitigate and cure human disease. These advances have most recently been acknowledged with Elissa Hallem's MacArthur Genius Grant, Dan Geschwind's Ruane Prize for Outstanding Achievement in Child and Adolescent Research, Alcino Silva's and Larry Zipursky's selection as Fellows of the American Association for the Advancement of Science, and Reggie Edgerton's award of the J. Allyn Taylor International Prize in Medicine. Such rewards also serve to validate the power of our interdisciplinary approach to neuroscience, and the value of our Affinity Groups, Integrative Centers for Excellence in Neuroscience, and the Joint Seminars in Neuroscience series. As these structured collaborations continue in the future, it is exciting to contemplate critical breakthroughs which will arise from the deepening engagement of creative scientific minds.

As I write this message though, I am also contemplating the looming reality of a monetary crisis that has, and will have a deep impact on the way we move forward in the future. On the macro level, Francis Collins (NIH) breaks it down in the November issue of JCI like this:

"*If Congress takes no action between now and January 2, 2013... that would mean an 8.2% cut in NIH support, which would be about $2.5 billion disappearing. This could be an extremely dark year for researchers... more like a 30% cut in the new and competing grant pool.*"

The figure to the right illustrates our rankings in context of the current grant funding, and captures our dominance at the National Institutes of Health within the NIDA, NIMH, and NINDS. This is a gratifying reflection of our research excellence, and a strong validation of the infrastructural strengths of our neuroscience community.



The grant pie may be shrinking, but I am confident that with our talent base, we are poised to maintain and even increase our portion of it.

At the University level, we are also faced with new challenges. Fall Quarter began with significant cuts to the California NanoSystems Institute, which hosts the several high-tech cores including the Advanced Light Microscopy Core, which combined with the Carol Moss Spivak Core several years ago. Fall Quarter is ending with dissolution of the UCLA Transgenic Core Facility, which has provided the transgenic and gene targeted animal models central to BRI research. This is during the same period that former facility director Meisheng Jiang has made real advances that will allow significant reductions in the cost of production of transgenic rat models, a development with potentially large impact on neuroscientific research on an international scale. One of my jobs is to protect the cores that are driving BRI member research, and despite external forces we will continue to find creative ways to do so.

Creative approaches to the challenges of 2013 are the key to overcoming them. As we look ahead to the holiday break, I want to remind our members, our alumni, our students, and our friends, that the BRI and its faculty comprise a world class institute. We consistently rank within the top 10 research institutes in the world, and in some areas we fall within the top 3. Our faculty is without peer in terms of commitment to its research mission and endgame, and our alumni such as Washington University Assistant Professor Paul Gray, are graduating to populate the next generation of prominent neuroscience researchers and teachers. 2013 will witness the survival of our exceptional core facilities despite a leaner operational context, and the advancement of fundamental breakthroughs such as those that happened only weeks ago.

Have a restful break. I look forward to seeing what we can accomplish together in the new year.

Paul Mathews from the laboratory of Tom Otis, presents the Arnold Scheibel Distinguished Postdoctoral Fellow in Neuroscience Lecture: "Using optogenetics to examine cerebellar circuits"

Paul Mathews obtained his Bachelor of Science degree with honors from the University of Oregon, and a Ph.D. degree from the University of Texas in Austin, where his research focused on how voltage gated ion channels contribute to the computational power of specific auditory brainstem neurons. His mentor at UT Austin recommended UCLA and the laboratory of BRI member Professor Tom Otis as a destination for his postdoctoral studies.

Mathews was intrigued by Otis' use of optogenetics and dynamic optics to explore the structure and interconnections of different brain circuits. Optogenetics is a technique to manipulate cell functioning at millisecond-levels of precision, by tagging cells with light-sensitive molecules that can then be stimulated to trigger on and off switches in the cells (i.e. ion channels, enzymes).

Mathews became particularly interested in the functional links between the climbing fibers and molecular layer interneurons in the cerebellar circuits. It's a question with particular historic resonance in this case: one of the first scientists to examine these circuits was Dr. Arne Scheibel, the former BRI Director, after whom the Distinguished Postdoctoral Fellow in Neuroscience Lecture is named.

Q: What about the climbing fiber pathway drew your attention as an area to study?

The cerebellum, whose role has been most associated with fine motor movement, receives only two major inputs. The first is the mossy fiber pathway that transmits information from sensory systems and the second is the climbing fiber pathway. The climbing fiber pathway is believed to signal errors in motor behavior, and subsequently drive the changes in the cerebellum necessary for motor learning. Recent work suggests that the changes necessary for motor learning in the cerebellum take place at multiple sites within the circuit. To gain a better understanding as to how and where climbing fibers drive these changes within the circuit, we have developed an optogenetic approach that allows us to specifically manipulate this element of the circuit. I believe this capability now gives us a good chance at answering many questions regarding the role of the climbing fiber pathway in cerebellar forms of motor learning.

Dr. Paul Mathews

Q: What were you hoping an optogenetic approach would tell you?

The optogenetic approach overcomes many of the technical challenges that arise during electrical stimulation, the technique classically used to manipulate neuronal activity on short time scales. My hope was that we would be able to develop a tool that would allow us to activate the climbing fiber pathway while recording from other neurons in the circuit to examine its effects on those cells. We've found that our viral approach to inserting the light activated molecules in climbing fibers works as well as we could have hoped.

Q: What were the important results? Were there any surprises?

We have demonstrated the specificity and utility of our optogenetic approach in controlling the climbing fiber pathway. We have successfully used this method to probe the impact of climbing fiber activation on different elements within the cerebellar circuit, especially those other than the classically described connection to Purkinje neurons. In particular we've shown in a paper, soon to be in press in the *Journal of Neuroscience*, that climbing fibers can increase the activity of local inhibitory interneurons within the cerebellar cortex. Activation of these inhibitory neurons leads to modulation of the output of the cerebellar cortex in a manner I believe is important for motor learning and memory. I guess you could say we were surprised as to the robustness of the response between climbing fibers and molecular layer interneurons.

Q: What is the "big picture?" of this research, in terms of how we understand the brain and/or learning and memory?

The research I've conducted has utilized an approach that allows one to control specific types of brain cells, or neurons with light. Using both viral and genetic techniques, we are now able to control the activity of a number of different neurons in the cerebellum, which plays a key role in motor coordination as well as some cognitive skills. There are a number of diseases that affect this brain region, and they often result in deficits in motor coordination termed ataxias. Through this research we hope to gain a better understanding as to how the cerebellar circuit shapes motor behavior as well as identifying the mechanisms underlying the cellular changes that take place during motor learning and memory. I have conducted experiments that illustrate how, through optical control of neurons in the cerebellum, one can measure the direct effects of these changes in other cerebellar neurons in a dish as well as monitor motor behavior and motor learning in awake behaving animals. Only through gaining insight into how different circuit elements contribute to coordinated movements through experiments like these will we be capable of developing targeted approaches to alleviating the symptoms that accompany cerebellar diseases.

Q: Where do you go from here?

I am currently working to expand the repertoire of cell types that can be controlled with light. Future experiments will use these techniques to manipulate specific types of neurons not only to examine how they affect other neurons within the circuit, but to also determine how changing their activity effects both motor behavior and motor learning.

Dr. Kate Wassum: from ARCS Scholar to UCLA Faculty

For many students, receiving a scholarship is a welcome validation of their academic abilities, and can provide the kind of financial security that allows them to focus on their studies. For Kate Wassum, the ARCS (Achievement Rewards for College Scientists) Fellowship she received at the beginning of her Ph.D. studies at UCLA was a turning point in a career just begun.

Wassum is now an Assistant Professor in the Department of Psychology, with a lab of her own where she is investigating the neurochemistry of decision-making. In 2005, as a newly accepted Ph.D. candidate at UCLA, she was unsure of where her studies would take her. Being awarded an ARCS Fellowship was an affirmation of her potential, but turned into much more. "It was a nice boost of confidence, when I started," says Wassum, adding that it was also an unexpected one: like all ARCS scholars, she had not applied for the award. Instead, it was granted on the strength of her application to UCLA's NSIDP (Interdepartmental Ph.D. Program for Neuroscience) program.

Wassum admits that not having to worry about rent was a welcome relief, but adds that the financial support was not so much a personal benefit as it was a professional one. She explains that the funding an ARCS scholar receives is not tied to a particular research question, but is a discretionary award belonging to the scholar. This means that they are not dependent on any given faculty member's ability to fund a student, and means that students are free to choose the field of neuroscience that most inspires them. "If you can work with whomever you want, you can be more passionate about what it is you are investigating," says Wassum.

Dr. Wassum now leads her own lab, but remains a supporter of the ARCS Foundation.

Dr. Kate Wassum is grateful for ARCS Foundation support.

She recently spoke at an ARCS-UCLA luncheon, honoring the newest group of ARCS Fellows: Patrick Chen; Theresa Harrison; Leanna Hernandez; Sarah Hersman; Donald Julien; Anna Parievsky; and Matthew Schreiner. She also had the opportunity to meet many of the generous donors who make the ARCS Foundation possible. "I was really impressed with the current ARCS scholars – they were all incredibly articulate about their research interest, and what ARCS Foundation support will mean for them," she says.

Dr. Wassum received support from the ARCS Foundation from 2005 until 2008, at which point she was awarded external funding from a UC training grant and a predoctoral training fellowship from NIDA. But even this subsequent funding was built on the "stamp of approval" in name recognition she'd earned from the ARCS Foundation.

"[An ARCS Fellowship] is a nice line item on your CV that people recognize, so when you send out applications for grants, reviewers can tell that you've already been proven and vetted. I think it was key for getting subsequent funding," explains Wassum.

Dr. Wassum had considerable success during her doctoral thesis studies and postdoctoral studies at UCLA, earning the Eva Mary Kavan Prize for Excellence in Research on the Brain in 2010 (an endowed award given annually to a UCLA neuroscience graduate student), and as the Arnold Scheibel Distinguished Postdoctoral Fellow in Neuroscience Lecturer the following year. She joined the UCLA faculty later in 2011.

Dr. Wassum's research has focused on the mechanisms governing reward and motivation in the brain. She demonstrated that the seemingly related phenomena of pleasure and desire were not inextricably linked, but involve the expression of endorphins in different brain regions. Her investigations included real-time observations of dopamine and glutamate expression to tease out their respective roles in the brain's reward pathways. The results have important implications in understanding addiction.

BRI Director Chris Evans was delighted that Dr. Wassum was hired by UCLA, and subsequently joined the BRI as a faculty member. "Kate's career at UCLA – starting with her Ph.D. studies, through her postdoctoral fellowship and her appointment to our faculty – is an excellent example of what we at the BRI hope to achieve with our education programs. The support that the ARCS Foundation provides to promising scholars like Kate is critical to the success of our mission."

Paul Gray presents the inaugural UCLA Neuroscience Graduate Student Alumni Lecture: "Selfish Networks: Development and Evolution of Simple Behaviors"

On December 11th, Dr. Paul Gray, Assistant Professor of Anatomy and Neurobiology at Washington University School of Medicine, delivered the inaugural address of the annual UCLA Neuroscience Graduate Student Alumni Lecture. Dr. Gray's undergraduate and graduate work at UCLA exemplifies his exceptional intellectual ability in, and personal commitment to, UCLA Neuroscience.

After postdoctoral appointments at Harvard and the Salk Institute, Dr. Gray was recruited to the faculty at Washington University in St. Louis. His academic career has led to a remarkable body of original research, which is of exceptional importance to our understanding of the sites and mechanisms underlying the generation of respiratory rhythm. Over the past 15 years, some of his papers have become the most highly cited works in his field.

Dr. Gray's lecture, "Selfish Networks: Development and Evolution of Simple Behaviors," explored the genes, networks, and evolution of circuits responsible for basic behaviors such as breathing. Breathing, in mammals, is an essential behavior activating neurons within the hindbrain and requiring the coordinated output of multiple respiratory muscles, such as the diaphragm and abdominals.

Using a combination of electrophysiology, molecular genetics, and anatomy in transgenic mice, Dr. Gray's investigations have found that essential rhythms of breathing are generated by hindbrain neurons derived from progenitors expressing the transcription factor Dbx1. Conversely, the temporal coordination between different respiratory muscle groups is controlled by neurons derived from progenitors expressing the TF Atoh1 which themselves play no role in rhythm generation.

These genes are very old in evolutionary terms, but did the neural circuits they generate evolve at the same time? Dr. Gray has discovered that neurons developmentally identical to those essential for respiratory output in mammals are present in the hindbrains of both amphibians and teleost fish in regions previously proposed for the generation of vocal communication. Together these data suggest that evolutionarily conserved networks of neurons generate simple behaviors.

In his introduction to Dr. Gray's lecture, Dr. Jack Feldman, Distinguished Professor of Neurobiology and member of the BRI quoted from a reference letter he wrote in 1998: "I first met him as an undergraduate, when he took my section of the course: *Neuroscience – From Molecules to Mind*. He was the brightest student, in a class of around 100, and as a result of Paul's sterling performance in the neuroscience series and his own interest in research, I invited him to join an ongoing project. Most of my colleagues were impressed, and thought Paul was a superb graduate student… They were surprised when informed he was still an undergraduate. We were very fortunate that he decided to continue his studies at UCLA."

Dr. Gray's close collaborations with members of the BRI continue. Together with Dr. Feldman and others, he has co-authored a major review for the Annual Review of Physiology, 2013: "Understanding the Rhythm of Breathing: So Near yet so Far." Dr. Gray's work will surely continue to bring us closer to the comprehension of such a simple, life-giving behavior.

Brain Research Institute 2012 student and postdoctoral award winners

Each year, the BRI and Semel Institute, along with Fine Science Tools, presents its awards to UCLA students and postdoctoral scholars at the Annual Neuroscience Poster Session. This year's winners include:

UCLA Chapter of the Society for Neuroscience Graduate Student Travel Award:
Elizabeth Reynolds Losin, working with Dr. Mirella Dapretto

Brain Research Institute Arnold Scheibel Distinguished Postdoctoral Fellow in Neuroscience Lecture:
Paul Mathews, working in the laboratory of Tom Otis

Fine Science Tools Postdoctoral Scholar Travel Awards:
Ariana Anderson, working with Mark Cohen
Amynah Pradhan, working with Chris Evans
Sika Zheng, working with Douglas Black

Brain Research Institute and Semel Institute for Neuroscience & Human Behavior Undergraduate Student Travel Awards:
Xinran Cui, working with William Grisham
Oghomwen Igiesuorobo, working with Peyman Golshani
Matthew Kelley, working with Istvan Mody
Aradhna Mayalall, working with Joe Watson
Nehali Mehta, working with Joe Watson
Michael Scott, working with Jing Liang and Richard Olsen

Brain Research Institute and Semel Institute for Neuroscience & Human Behavior Graduate Student Travel Awards:
Aida Attar, working with Gal Bitan
Emily Barkley-Levenson, working with Adriana Galvan
Andrew Brumm, working with Tom Carmichael
Micah Chambers, working with Jack Van Horn
Zhiping Chen, working with Mayank Mehta
Martina DeSalvo, working with Kelsey Martin
Dylan Gee, working with Nim Tottenham
Stephanie Groman, working with David Jentsch
Rachel Jonas, working with Jamie Feusner
Wesley Kerr, working with Mark Cohen
Sarah Madsen, working with Paul Thompson and Joe Watson
Angelica Morales, working with Edythe London
Yatendra Mulpuri, working with Elizabeth Sowell
Katherine Myers, working with Felix Schweizer
Weisong Ong, working with James Bisley
Thomas Rogerson, working with Alcino Silva
Ariel Schvarcz, working with Carrie Bearden

Brain Research Institute and Semel Institute for Neuroscience & Human Behavior Postdoctoral Fellow Travel Awards:
Albert Barth, working with Istvan Mody
Luca Caracciolo, working with Tom Carmichael
Catalina Cervantes, working with David Jentsch
Martin Haustein, working with Baljit Khakh
Yong-Seok Lee, working with Alcino Silva
Vincent Marty, working with Igor Spigelman
Ian Mendez, working with Nigel Maidment
Shira Rosenzweig, working with Tom Carmichael
Nanthia Sultana, working with Barbara Knowlton
Anna Taylor, working with Chris Evans
Sara Wasserman, working with Mark Frye

Elissa Hallem is awarded the MacArthur Fellowship for unearthing the neuroscience of nematodes

Dr. Elissa Hallem (Photo courtesy of the John D. & Catherine T. MacArthur Foundation)

Every October, the John D. and Catherine T. MacArthur Foundation announces awardees of its coveted MacArthur Fellowship – a small group of artists and scientists from all over the world, whose career accomplishments and innate gifts are reflections of what the word "genius" truly means. This year, BRI member, Dr. Elissa Hallem, Assistant Professor of Microbiology, Immunology and Molecular Genetics, was one of 23 worldwide recipients of the MacArthur Fellowship, continuing an exceptional trajectory of accomplishments that began when she was a teenager, whose extra-curricular activities included working in the laboratory of a family friend.

The family friend happened to be Dr. Larry Zipursky, a UCLA faculty member in Biological Chemistry and BRI member, whose study of *Drosophila melanogaster* (or the common fruit fly) provides powerful insights into the molecular mechanisms through which nerve cells are wired together in the brain. "During high school, I was lucky to have three years to observe first hand what lab studies of *Drosophila* can accomplish, and learn about a lot of fascinating questions in neuroscience," Dr. Hallem says. After studying biology and chemistry at Williams College, Hallem reengaged with her study of *Drosophila* as a Ph.D candidate in neuroscience, studying with Dr. John Carlson at Yale. It was there that she began to explore the ramifications of olfactory perception in this insect system, identifying the stimuli that prompt olfactory receptors to activate or inhibit neuronal firing.

In the search for clarity in articulating the specific features of neural circuits that give rise to behavioral output, Dr. Hallem began working with nematodes – free-living and parasitic worms. "The strength of worms as a model system is that the interaction between signaling pathways and neural circuits is relatively easy to study. We're interested in using worms to understand how sensory neural circuits evolve to give rise to species-specific behaviors," she explains. Though the free-living worm *C. elegans* is an established animal model, Hallem's work also utilizes a broad range of non-model species. Her lab conducts large scale screens for olfactory preferences, and studies the neural circuits that underlie these preferences.

"Worms have very strong likes and dislikes when it comes to odors," she says. They are also optically transparent, with only about 300 neurons despite the wide spectrum of behavioral repertoires between species.

While the *C. elegans* animal model is certainly a mainstay in neuroscience literature, far fewer people work with the numerous species of parasitic worms that Dr. Hallem investigates, partially because they are very difficult to grow. "In many cases, parasitic worms are very different from *C. elegans*. It takes time to establish lab protocols and interpret the behavior for each of the species I work with, many of which have never been studied in this context," she says. Once protocols and behavioral assays have been refined, Hallem hopes to use calcium imaging techniques to identify the neural activity patterns accompanying the behavior of the odor-driven free-living and parasitic worm species under study.

Dr. Hallem's work could have an enormous benefit to human and ecological health in the future. Parasitic worms pose a major threat to human health and are endemic in many parts of the developing world. By better understanding chemoreception in various species – specifically, how infective juveniles sense carbon dioxide and other odors in order to locate host organisms to invade – Dr. Hallem hopes to contribute to a means of limiting the effect of current and future scourges. The right olfactory data may lead to interventions preventing parasitic infections in humans, such as DEET-style repellents, or mosquito-style odor traps. "We have drugs that cure parasitic infections, but as soon as medication ceases, reinfection occurs. With targeted studies of parasitic worm behavior, we may be able to prevent infection in the first place," she says. Hallem's work could also mitigate the need for some chemical pesticides. "We also study insect-parasitic nematodes that are used as biocontrol agents for many agricultural pests. Using olfactory cues to attract these worms to the right environments could improve their efficacy as biocontrol agents."

The MacArthur Fellowship support could go a long way to furthering Hallem's research missions. The Fellowship is worth $500,000 over a five year period and there are no strings attached in terms of what questions researchers can pursue with Foundation support. To Dr. Hallem's knowledge, "no one else is studying the sensory neurobiology of parasitic worms, and it's invaluable to have an award that allows for the pursuit of riskier, less developed ideas in a relatively new area of study."

Though she doesn't like the word "genius", one can visualize Dr. Hallem as an intense young teenager in Dr. Zipursky's lab, imagining a myriad of pathways leading to her ultimate goal – contributing a breakthrough that would lead to an improvement in human health. While originally inspired by Dr. Zipursky, who is now a Distinguished Professor of Biological Chemistry and Investigator in the Howard Hughes Medical Institute, Dr. Hallem has become a UCLA faculty member leading her own lab, well on the path toward such a breakthrough.

Twenty-fourth Annual Neuroscience Poster Session

The 24th Annual BRI Neuroscience Poster Session, in which UCLA neuroscientists share their research with one another and the university neuroscience community, was held in the Ackerman Union's Grand Ballroom on December 4, 2012.

Fine Science, Fine Scholars

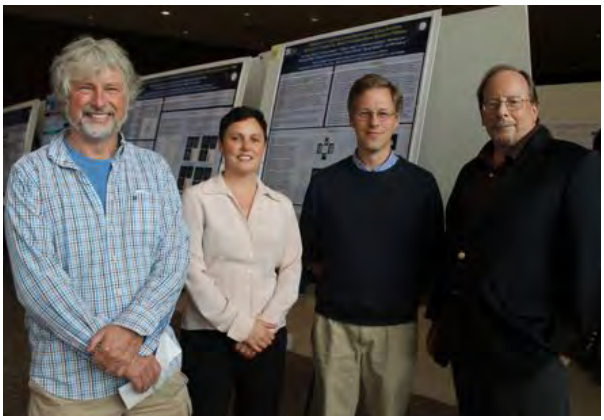
The Annual BRI Neuroscience Poster Session is an opportunity to recognize the achievements of postdoctoral scholars. Here, Christina Callanta (second from left), Fine Science Tools Technical Support and Customer Relations Manager, stands with Fine Science Tools Postdoctoral Scholar Travel Award recipients (l to r): Sika Zheng, Ariana Anderson and Amynah Pradhan. Fine Science Tools is a long-time sponsor of these awards and of the BRI's Annual Poster Session (more award winners on page 4).

Carl Zeiss Microimaging, a sponsor of the Poster Session, displayed their latest products and services at the event.

Poster Session Distinguished Lecturer, J. Anthony Movshon

BRI Director Dr. Chris Evans (left) greeted the Annual Neuroscience Poster Session's Distinguished Lecturer, J. Anthony Movshon of New York University's Center for Neural Science (right). Dr Movshon's talk was entitled "Cortical Mechanisms of Visual Perception."

He was hosted by Drs. Michele Basso (second from left) and James Bisley (third from left).



The Annual BRI Neuroscience Poster Session is traditionally held after the Annual Meeting of the Society for Neuroscience, to provide the opportunity for neuroscience students, postdocs and faculty to learn about one another's research in a more intimate setting.

This year, there were 160 posters on display.

The Transgenic Core — in survival mode

In a recent interview featured in the November issue of the *Journal for Clinical Investigation*, Dr. Francis Collins, Director of the National Institute of Health, spoke about the state of NIH funding in real terms. "[Since 2003] funding support for biomedical research has gone flat and inflation has eroded it further – we now actually have about 20% less in terms of resources to put into medical research than we did 10 years ago." Despite this, the faculty and research staff of the BRI have maintained the standards of excellence characterizing the institute since its inception over 50 years ago. The success of BRI faculty grant applications, as discussed in the Director's Message, is outstanding. However, there are imminent challenges to come.

Dr. Collins continues: "[The erosion in funding] is extremely frustrating when you see the potential for breakthroughs that we are trying to pursue and that could be achieved so much faster." Collins' frustration has been particularly resonant in recent weeks, in the context of maintaining a UCLA Transgenic Facility providing research investigators with transgenic and gene-targeted animals.

The importance of this core resource in the context of biomedical research is clear. As basic and clinical neuroscience focuses on the study of genetic bases of diseases and disorders, models that specify pathways of pathogeneses are essential for implicating the causal, dysfunctional neural systems. The more refined the molecular genetic methods to create animal models, the better understanding we will have of genetic factors contributing to human disease and eventually clinical interventions. But with a dismal fiscal climate upon us, many cores, including our Transgenic Core, are under a fiscal microscope. Where at all possible, costs are being trimmed by melding technical services within and between universities in an effort to save costs and avoid duplicative resource allocation. It seems much of the UCLA Transgenic Core's business will now be outsourced. Although the trimming has good budgetary intentions, at least in the short term, the loss of the core has faculty concerned about the ability of UCLA to remain competitive for funding, and attract and retain colleagues reliant on transgenic rodents for their research.

It has only been 30 years since researchers discovered the ability to isolate mouse embryonic stem cells which can develop into the full range of tissues, and only since 1987 that the first knockout (KO) mice were produced. At present, transgenic animals are ubiquitous reagents in neuroscience research worldwide – but production certainly has its limitations. The most widely used transgenic model production technique uses a pronuclear injection of plasmid DNA into fertilized oocytes. It is most successful in mice, but even then transgenic rates usually range from 2% to 10%, predicating the need to repeat the process until founder animals are established. This puts further limits on the viability of other animal models because the larger the animal, the higher the cost, and the less efficient the result. At the same time, the physiological traits of larger animals such as rats are significantly more homologous with humans, and thus are significantly more utile for neuroscientific investigations.

In November, Dr. Meishang Jiang, Director of the UCLA Transgenic Facility at the time, perfected an application of a new technology that has the potential to make a significant step forward in the production of a viable transgenic rat model. For several years now, a growing body of researchers has begun to use lentiviral (LV) vectors in development of a prototype for transgenic production. Otherwise known as complex retroviruses, LVs are part of the viral vector system developed for application in gene therapy to correct human immunodeficiency disorders. LV plasmid components seamlessly integrate into mammalian genomic DNA, providing an ideal format in which to modify cells *in vitro* and *in vivo*. For the past year, Dr. Jiang has used LV technology in mouse models, and discovered a 50-70% increase in efficiency based on transgenic success rates, thus resulting in the use of fewer animals to achieve research goals. Before the Transgenic Core lost its funding, Dr. Jiang had hoped to use the lentivirus technique to produce transgenic rats. For UCLA researchers, this would have meant at least a 50% reduction in cost for transgenic rat models, giving BRI members a distinct advantage over most other research institutions. As Dr. Jiang put it: "We have improved the lentivirus based method in mice, and it works beautifully. Nobody else generates transgenic rats on campus, and we have perfected the technology to do so."

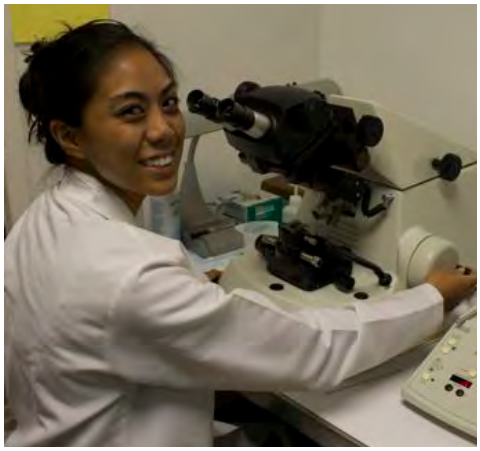
Coterminous with the development of LV methodology, the Transgenic Facility adapted a breakthrough technique for manipulating the genome. "In the context of gene therapy, researchers traditionally use classical recombinant methodology to develop the vectors to correct mutations in stem cells. This process is imperfect, like ripping a photo in half and taping it back together," Dr. Jiang explained. When DNA is microinjected into cells, cellular structure can be compromised. This prompts cells to attempt auto-repair in a process that can generate even more deletions in the genome. Transcription Activator-Like Effector Nucleases (TALENs) have the potential to solve this problem. Put simply, the TAL receptor is a bacteria-secreted protein with amino acids that can specify DNA bases in the TAL effector's target site. Researchers have used this capacity to specifically design TALENs that can cleave to a specific DNA sequence. "TALENs simplify the transgenic knockout process. We tested the design in stem cells, on zebrafish, and on mice. The protocol works, and could provide us with a very powerful tool in production of transgenic rats," Dr. Jiang said in late November. "I am excited to work with this new technology, and look forward to providing it for UCLA researchers."

On December 5, 2012, the David Geffen School of Medicine/ UCLA Health System announced a significant reduction in the services and functions of the Transgenic Core, due to fiscal pressures at the University, State and Federal levels. Though Dr. Jiang remains affiliated as a scientific consultant, the Core will outsource much of its services to the Mouse Biology Program at Davis. On the verge of providing UCLA neuroscientists with new, efficient and affordable mouse and rat models, the Transgenic Facility has been forced to take a long pause in its drive toward innovation. Instead it must focus on survival, and perhaps facilitate the emergence of grass-root efforts to revive selective aspects of the core.

Despite lean times, the Electron Microscopy Facility remains on call for UCLA scientists

Above: EM Microscopy Services Center supervisor Dr. Sirus Kohan at the console of the JEOL 100CX.

Below: Technician Kristina Takahashi at the core facility's microtome.



As the supervisor of the Brain Research Institute's Electron Microscopy (EM) Services Center, Dr. Sirus Kohan and other staff of the EM facility have a hand in an impressively broad range of research publications every year. It's one benefit of running a facility that provides centralized electron microscopy expertise for UCLA scientists.

Researchers interested in adding electron microscopy to their research need only dissect and fix the tissues they want examined, and deliver them to the sixth floor of the CHS building. Kohan and core staff member Birgitta Sjostrand complete the remaining processes of preparation and deliver samples ready for analysis. "It will take you at least a year to train a postdoc or student in the preparation of samples for electron microscopy. But everything is ready here," says Kohan. "We prepare the samples, and when the sections are ready for analysis we notify the researchers. We also provide training in the use of the electron microscope. Acquired images can then be used to support grant applications, publications or for any other purpose".

According to Kohan, the microscope – a JEOL 100CX – is relatively straightforward to use and can provide images of up to 200,000 magnification. In addition, the EM Core also offers the use of a Reichert Ultracut Microtome, together with the expertise of technician Kristina Takahashi. Kohan estimates that roughly half of the EM Core's clients are BRI members, with the remainder coming from other departments. Consequently, the 6th floor JEOL has scrutinized samples from the simplest microorganisms to tissues from every organ system.

BRI member, Dr. Uptal Banerjee, is a recent client of the EM Core. He approached the facility when he was unable to discern the exact phenotype of an oncogenetic expression in *Drosophila mitochondria* using conventional florescent microscopy. "We found the facility very helpful for our research project. We approached the facility wanting to have thin sections of *Drosophila* tissues. Given the small size of the tissues and the specific requirements of our experiments, it was a challenge to obtain thin sections of these tissues. But the staff at the facility were kind and patient, and willing to make an extra effort to solve the problem. In the end, we were able to dissect out our mitochondrial phenotype and make definitive conclusions," says Banerjee.

Situations like Banerjee's are not uncommon, but Kohan said that the facility is capable of incorporating researchers' scientific goals from their inception. "Researchers with future plans to use the EM Core may believe the best approach is to outsource funding and hire someone for the task. However, we encourage them to consider using our services. In many instances we can do the job at a fraction of the cost".

For more information on the EM Core, contact Core Supervisor, Sirus Kohan, Ph.D., sakohan@ucla.edu; 310-206-8054 or online at http://www.bri.ucla.edu/

Major donation to brain tumor research at UCLA

Brain tumor research at UCLA received a big boost, thanks to the generosity of Ted Gagliano, a senior executive with 20th Century Fox Studios. Mr. Gagliano contributed $1 million that will support the research of BRI member, Dr. Linda Liau, whose innovative tumor-vaccines show real promise as an effective treatment in glioblastoma therapy.

Dr. Linda Liau and Ted Gagliano

Gagliano explained that he had been invited to attend last year's UCLA Neurosurgery's Visionary Ball. The testimonies of former neurosurgery patients there inspired Gagliano – who had a close friend undergoing surgery for a brain tumor that same evening – to support the program. "I was moved by the unfairness of brain disease, and it hit me how lucky I am to be healthy. I learned about the great work that UCLA does and wanted to do more to help," he told a UCLA Newsroom reporter.

It was a tour of Dr. Liau's lab that confirmed Gagliano's decision to donate to UCLA. "What excites me is the chance to offer cancer patients a promising treatment that gives them hope and makes their lives better. That's why I was fascinated by Dr. Liau's vaccine work. She isn't just surgically removing brain tumors; she's looking for new ways to stop them in their tracks for good. I wanted to support research that she wouldn't be able to do otherwise."

Neuroscience *Quotables*

"Science is becoming increasingly interdisciplinary and transdisciplinary, and psychoneuroimmunology has been in that forefront now for two decades."

~ Michael Irwin, Professor of Psychiatry and Biobehavioral Sciences, quoted in an August 3 article in *Psychiatric News* on the burgeoning field of psychoneuroimmunology.

"Drug abuse treatment developed outside mainstream medicine… We're still suffering from that."

~ On September 22, a *Los Angeles Times* article quoted Walter Ling, Professor of Psychiatry and Biobehavioral Sciences, about the challenges scientifically-based medical interventions for drug addictions face in the context of 12-step style behavioral treatment programs.

"There's no doubt that some of the best research groups in the world didn't get re-funded, and they should have."

~ Susan Bookheimer, Joaquin Fuster Chair in Cognitive Neurosciences was quoted by the *Pittsburgh Post-Gazette* on October 2 about recent federal decisions regarding cuts in autism research funding. The UCLA Autism Center for Excellence was the only center out of six to receive renewal funding from the NIH.

"If you manipulate something at the gut level, this will be reflected at the brain level."

~ Emeran Mayer, Professor of Medicine, Psychiatry and Biobehavioral Sciences, confirms that the best way to a person's mind is through their stomach in a September 13 article in the *Los Angeles Times* on the role of gut microbes in promoting health and treating disease.

Congratulations

The renowned John D. and Catherine T. MacArthur Foundation has named Dr. **Elissa Hallem** one of their 2012 MacArthur Fellows. See the feature article on page 5 in this edition.

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The Brain and Behavior Research Foundation (BBRF) has named Dr. **Daniel Geschwind**(right) as one of the recipients of this year's Ruane Prize for Outstanding Achievement in Child and Adolescent Research.

The Ruane Award is meant to recognize an outstanding scientist seeking to understand the causes, pathology or treatment of childhood mental illness. It has been given annually since 2000.

Dr. Geschwind was an obvious choice for the award. The Gordon and Virginia MacDonald Distinguished Chair in Human Genetics is a Professor of Neurology and Psychiatry at the UCLA School of Medicine, and is widely known as one of the foremost researchers in the world on autism.

Applying a broad spectrum of approaches to analyze the complex genetic underpinnings of autism and how they are expressed in the brain, Geschwind is dedicated to applying this knowledge in order to identify therapeutics to treat and alleviate the effects of this widespread disorder.

In addition to his groundbreaking work in the lab, Dr. Geschwind is also director of the Center for Autism Research and Treatment (CART), co-director of the Center for Neurobehavioral Genetics at UCLA, and was a driving force behind the creation of the Autism Genetic Resource Exchange.

The BBRF (formerly known as the National Alliance for Research on Schizophrenia and Depression) is one of the largest private foundations dedicated to funding research on mental health, having disbursed more that $300 million in grants in its quarter century of existence.

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Professor **Alcino Silva** (left) of the Departments of Neurobiology, Psychiatry and Biobehavioral Sciences and Psychology, and **Larry Zipursky**, Professor in the Department of Biological Chemistry, and Investigator in the Howard Hughes Medical Institute, have been selected as Fellows of the American Association for the Advancement of Science (AAAS).

Dr. Silva was honored for "pioneering research in the field of molecular and cellular cognition, including seminal discoveries in the molecular basis of memory and cognitive disorders."

Dr. Zipursky (right) was honored for "distinguished contributions to the field of developmental neurobiology, particularly for discovering molecular mechanisms underlying the assembly of neural circuits."

The AAAS is one of the largest and most distinguished scientific societies in the world. Founded in 1848, the society has grown to become a leading advocate for science and education world-wide. They publish the journal *Science*, and seek to advance public understanding of scientific issues and defend research integrity nationally and internationally. Drs. Silva and Zipursky will be recognized at a special forum during the AAAS Annual Meeting in Boston early next year.

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V. **Reggie Edgerto**n (left), Distinguished Professor of Integrative Biology and Physiology, and Neurobiology, was awarded the J. Allyn Taylor International Prize in Medicine by the University of Western Ontario's Schulich School of Medicine & Dentistry's Robarts Research Institute in November, for his groundbreaking spinal cord research spanning 30 years.

Dr. Edgerton and colleagues were also awarded a Popular Mechanics' 2011 Breakthrough Award for developing "an electric therapy that stimulates spinal nerves, allowing the paralyzed to walk." Edgerton has been studying the effects of electrical stimulation on the spinal cord for more than 30 years and, in 2011, his research team published on a significant breakthrough in their initial work with a paralyzed male volunteer in the British medical journal *The Lancet* - the result of 30 years of research to find potential clinical therapies for paralysis.

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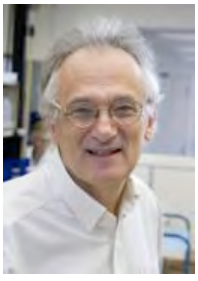


Steven G. Clarke (right), Distinguished Professor in the Department of Chemistry and Biochemistry, has been named to UCLA's Elizabeth and Thomas Plott Chair in Gerontology.

The endowed chair, held for a five-year term, is intended for a scholar who conducts research and education activities related to aging and longevity in the areas of molecular biology, neuroscience and immunology.

An authority in his field, Clarke focuses on the biochemistry of the aging process and conducts research aimed at understanding, on a molecular level, how human functions are maintained during aging. For more, read here: http://newsroom.ucla.edu/portal/ucla/ucla-chemist-named-to-endowed-237840.aspx

Research Briefs

Women with sleep apnea have higher degree of brain damage than men

Women suffering from sleep apnea have, on the whole, a higher degree of brain damage than men with the disorder, according to a first-of-its-kind study conducted by researchers at the UCLA School of Nursing. The findings are reported in the December issue of the peer-reviewed journal *SLEEP*.

Obstructive sleep apnea is a serious disorder that occurs when a person's breathing is repeatedly interrupted during sleep, sometimes hundreds of times. Each time, the oxygen level in the blood drops, eventually resulting in damage to many cells in the body. If left untreated, it can lead to high blood pressure, stroke, heart failure, diabetes, depression and other serious health problems.

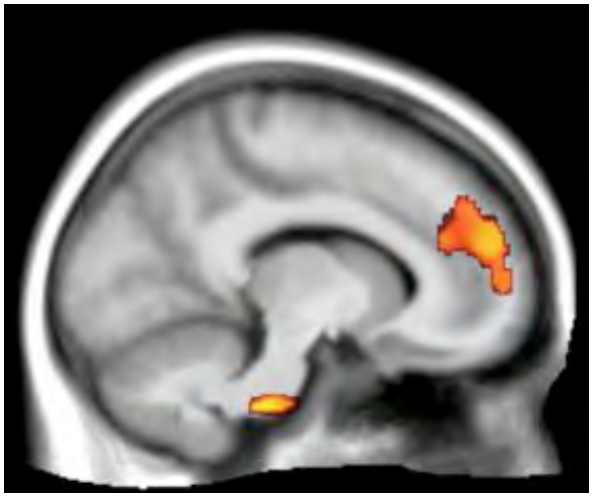


Image shows areas of the brain in which women with sleep apnea are particularly impacted.

Approximately 10 years ago, this UCLA research team was the first to show that men with obstructive sleep apnea have damage to their brain cells. For this latest, multi-year study, "Sex Differences in White Matter Alterations Accompanying Obstructive Sleep Apnea," the researchers looked at patients who were diagnosed with obstructive sleep apnea at the UCLA Sleep Laboratory. They compared the nerve fibers in these patients' brains — known as white matter — to fibers of individuals without sleep problems and focused on unearthing the difference in brain damage between men and women with sleep apnea.

"While there are a great many brain studies done on sleep apnea and the impact on one's health, they have typically focused on men or combined groups of men and women, but we know that obstructive sleep apnea affects women very differently than men," said chief investigator Paul Macey, assistant professor and associate dean of information technology and innovations at the UCLA School of Nursing. "This study revealed that, in fact, women are more affected by sleep apnea than are men and that women with obstructive sleep apnea have more severe brain damage than men suffering from a similar condition."

In particular, the study found that women were impacted in the cingulum bundle and the anterior cingulate cortex, areas in the front of the brain involved in decision-making and mood regulation. The women with sleep apnea also showed higher levels of depression and anxiety symptoms, the researchers said. "This tells us that doctors should consider that the sleep disorder may be more problematic and therefore need earlier treatment in women than men," Macey said.

With this finding as a foundation, Macey said that the next step is for researchers to "untangle the timing of the brain changes" and find out if treating sleep apnea can help the brain. "What we don't yet know," he said, "is, did sleep apnea cause the brain damage, did the brain damage lead to the sleep disorders, or do the common comorbidities, such as depression, dementia or cardiovascular issues, cause the brain damage, which in turn leads to sleep apnea."

Co-investigators on the study included Rajesh Kumar, Ronald Harper and Dr. Frisca Yan-Go of UCLA's Brain Research Institute and the departments of neurobiology and neurology at the David Geffen School of Medicine at UCLA, and Mary Woo of the UCLA School of Nursing. All of the work for the study was performed at UCLA, with financial support provided by a grant from the National Institute of Nursing Research. -- *Laura Perry, UCLA Newsroom*

Breast cancer and depression: UCLA gets $5M to study why survivors are at such high risk

UCLA researchers have received a $5 million grant from the National Cancer Institute for a study aimed at developing a risk profile for breast cancer survivors likely to suffer from depression. The prevalence of depression among survivors is three to five times greater than in the general population.

UCLA will be teaming on the five-year study with Kaiser Permanente, which will provide the 300 volunteers needed for the study by culling through electronic patient records to locate women who have been treated for breast cancer and have not had a history of depression.

Researchers believe that cancer and its treatment induce inflammation, which in turn leads to sleep disturbance and depression. Sleep disturbance occurs in more than half of breast cancer survivors and is thought to contribute to the elevated risk of depression in these women. Depression negatively impacts quality of life and increases the risk of death, possibly due to an increased chance of cancer recurrence.

Through the study, researchers hope to find out if certain sub-sets of breast cancer survivors are at greater risk for depression by examining their DNA for potential biomarkers and genetic anomalies. If they can identify a risk profile, a study would be launched later to evaluate prevention measures, said the study's principal investigator, Dr. Michael Irwin, a professor of psychiatry and biobehavioral sciences at the Cousins Center for Psychoneuroimmunology, part of the Semel Institute for Neuroscience and Human Behavior at UCLA.

"Depression in breast cancer survivors is a huge problem. It often goes undiagnosed and is undertreated," Irwin said. "If we can identify those breast cancer survivors at elevated risk for sleep disturbance and, therefore, depression, we can diagnose and treat it earlier, with better outcomes. Additionally, if we can identify those at greatest risk, efforts can be implemented early to prevent the occurrence of depression in the first place. "Because depression is so prevalent and difficult to treat in breast cancer survivors, prevention of depression will dramatically improve the quality of their life." -- *Kim Irwin, UCLA Newsroom*

For more see: http://newsroom.ucla.edu/portal/ucla/ucla-researchers-awarded-5-million-240554.aspx

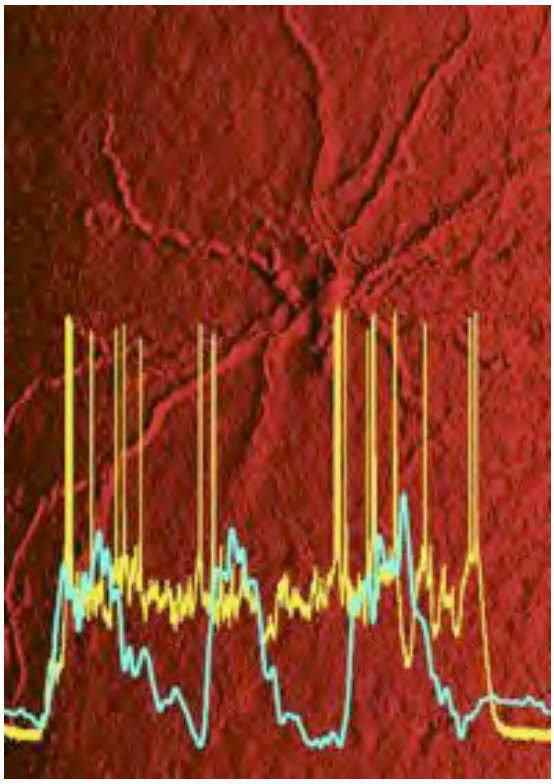
UCLA scientists discover sleeping brain behaves as if it's remembering something

UCLA researchers have for the first time measured the activity of a brain region known to be involved in learning, memory and Alzheimer's disease during sleep. They discovered that this region, called the entorhinal cortex, behaves as if it's remembering something, even during anesthesia-induced sleep — a finding that counters conventional theories about sleep-time memory consolidation.

The research team simultaneously measured the activity of single neurons from multiple parts of the brain that are involved in memory formation. The technique allowed them to determine which brain region was activating other areas and how that activation was spreading, said the study's senior author, Mayank R. Mehta, a professor of neurophysics in UCLA's departments of neurology, neurobiology, and physics and astronomy.

In particular, Mehta and his team looked at three connected brain regions in mice — the neocortex, or "new brain," the newest part of the cerebral cortex to evolve; the hippocampus, or "old brain"; and the entorhinal cortex, an intermediate brain that connects the new and the old brains.

While previous studies have suggested that the dialogue between the old and the new brain during sleep was critical for memory formation, researchers had not investigated the contribution of the entorhinal cortex to this conversation, which turned out to be a game-changer, Mehta said.



In the background is an entorhinal cortex neuron that was studied. The blue-green trace shows neocortical slow oscillation while the yellow trace shows the persistent activity of entorhinal cortical neuron, even when the inputs from neocortex were silent.

Mehta's team found that the entorhinal cortex showed what is called persistent activity, which is thought to mediate working memory during waking life — for example, when people pay close attention to remember things temporarily, such as recalling a phone number or following directions. "The big surprise here is that this kind of persistent activity is happening during sleep, pretty much all the time," Mehta said. "These results are entirely novel and surprising. In fact, this working memory–like persistent activity occurred in the entorhinal cortex even under anesthesia."

The study appears Oct. 7 in the early online edition of the journal *Nature Neuroscience*. The findings are important, Mehta said, because humans spend one-third of their lives sleeping, and a lack of sleep results in adverse effects on health, as well as learning and memory problems.

It had been shown previously that the neocortex and the hippocampus "talk" to each other during sleep, and it is believed that this conversation plays a critical role in memory consolidation, the establishing of memories. However, no one had been able to interpret the conversation. "When you go to sleep, you can make the room dark and quiet, and although there is no sensory input, the brain is still very active," Mehta said. "We wanted to know why this was happening and what different parts of the brain were saying to each other."

Mehta and his team developed an extremely sensitive monitoring system that allowed them to follow the activities of neurons from each of the three targeted portions of the brain simultaneously, down to the activity of a single neuron. This allowed them to decipher the precise communications, even when the neurons were seemingly quiet. They then developed a sophisticated mathematical analysis to decipher the complex conversation.

During sleep, the neocortex goes into a slow wave pattern for about 90 percent of the time. And during this period, its activity slowly fluctuates between active and inactive states about once every second.

Mehta and his team focused on the entorhinal cortex, which has many parts. The outer part mirrored the neocortical activity. However, the inner part behaved differently. When the neocortex became inactive, the neurons in the inner entorhinal cortex persisted in the active state, as if they were remembering something the neocortex had recently "said," a phenomenon known as spontaneous persistent activity.

Further, they found that when the inner part of the entorhinal cortex became spontaneously persistent, it prompted the hippocampus neurons to become very active. On the other hand, when the neocortex was active, the hippocampus became quieter. This data provided a clear interpretation of the conversation.

"During sleep, the three parts of the brain are talking to each other in a very complex way," he said. "The entorhinal neurons showed persistent activity, behaving as if they were remembering something — even under anesthesia, when the mice could not feel or smell or hear anything. Remarkably, this persistent activity sometimes lasted for more than a minute, a huge time-scale in brain activity, which generally changes on a scale of one-thousandth of a second."

The findings challenge current theories of brain communication during sleep, in which the hippocampus is thought to talk to, or drive, the neocortex. Mehta's findings instead indicate that the entorhinal cortex is the third key actor in this complex dialogue and that the neocortex is driving the entorhinal cortex, which in turn behaves as if it is remembering something. That, in turn, drives the hippocampus, while other activity patterns shut it down.

"This is a whole new way of thinking about memory consolidation theory," Mehta said. "We found there is a new player involved in this process and it's having an enormous impact. And what that third player is doing is being driven by the neocortex, not the hippocampus. This suggests that whatever is happening during sleep is not happening the way we thought it was. There are more players involved, so the dialogue is far more complex, and the direction of the communication is the opposite of what was thought." -- *Kim Irwin, UCLA Newsroom*

See more see: http://newsroom.ucla.edu/portal/ucla/ucla-scientists-discover-that-239347.aspx

Researchers report potential new treatment to stop Alzheimer's disease


Dr. Gal Bitan

Last March, researchers at UCLA reported the development of a molecular compound called CLR01 that prevented toxic proteins associated with Parkinson's disease from binding together and killing the brain's neurons.

Building on those findings, they have now turned their attention to Alzheimer's disease, which is thought to be caused by a similar toxic aggregation or clumping, but with different proteins, especially amyloid-beta and tau.

And what they've found is encouraging. Using the same compound, which they've dubbed a "molecular tweezer," in a living mouse model of Alzheimer's, the researchers demonstrated for the first time that the compound safely crossed the blood–brain barrier, cleared the existing amyloid-beta and tau aggregates, and also proved to be protective to the neurons' synapses — another target of the disease — which allow cells to communicate with one another. The report appears in the current online edition of the journal *Brain*.

"This is the first demonstration that molecular tweezers work in a mammalian animal model," said Gal Bitan, an associate professor of neurology at UCLA and the senior author of the study. "Importantly, no signs of toxicity were observed in the treated mice. The efficacy and toxicity results support the mechanism of this molecular tweezer and suggest these are promising compounds for developing disease-modifying therapies for Alzheimer's disease, Parkinson's and other disorders."

Molecular tweezers are complex molecular compounds capable of binding to other proteins. Shaped like the letter "C," these compounds wrap around chains of lysine, a basic amino acid that is a constituent of most proteins. Bitan and his colleagues, including Aida Attar, first author of the study and a graduate student in Bitan's lab, have been working with a particular molecular tweezer called CLR01.

In collaboration with scientists at the Università Cattolica in Rome, the researchers, working first in cell cultures, found that CLR01 effectively inhibited a process known as synaptotoxicity, in which clumps of toxic amyloid damage or destroy a neuron's synapses. Even though synapses in transgenic mice with Alzheimer's may shut down and the mice may lose their memory, upon treatment, they form new synapses and regain their learning and memory abilities.

"For humans, unfortunately, the situation is more problematic because the neurons gradually die in Alzheimer's disease," Bitan said. "That's why we must start treating as early as possible. The good news is that the molecular tweezers appear to have a high safety margin, so they may be suitable for prophylactic treatment starting long before the onset of the disease." -- *Mark Wheeler, UCLA Newsroom*

For more see: http://newsroom.ucla.edu/portal/ucla/potential-new-treatment-to-stop-239289.aspx

Study reveals how common gene mutation affects kids with autism spectrum disorders

Over the past decade, researchers have made great strides in identifying genes that lead to an increased risk of autism spectrum disorders (ASD), which result in a continuum of social deficits, communication difficulties and cognitive delays. But it's still critical to determine how exactly these genetic risk factors impact the brain's structure and function so that better treatments and interventions can be developed.

This led researchers at UCLA to look more closely at one particular culprit that's known to cause a susceptibility to ASD — a genetic variant, or mutation, in the MET receptor tyrosine kinase gene, commonly known simply as MET.

And what they found was striking: For the first time, the researchers showed that the so-called "C" variant, which reduces MET protein expression, specifically impacts the network of connections among different areas of the brain involved in social behavior, including recognizing emotions shown on people's faces. While this gene variation is commonly found in the brains of both health individuals and those with ASD, the study showed that the gene has a bigger impact on brain connectivity in children with ASD. The findings appear in the current online edition of the journal *Neuron*.

Senior author Mirella Dapretto, a professor of psychiatry at the Semel Institute of Neuroscience and Human Behavior at UCLA; first author Jeff Rudie, a graduate student in Dapretto's lab; and Pat Levitt, the Provost Professor of Neuroscience, Psychiatry, Psychology and Pharmacy at the University of Southern California, who discovered MET's association with ASD, used three different types of magnetic resonance imaging (MRI) to determine how the MET risk factor impacts brain structure and function.

Their findings provide new insight into understanding ASD heterogeneity — the considerable individual differences in how ASD symptoms present — which has challenged the field in developing more effective diagnostic tools and biologically based interventions for all affected children. Eventually, genetic information may be useful in identifying subgroups of individuals with ASD who may better respond to different types of treatment. "Although researchers have begun to identify a variety of autism risk genes, the exact mechanisms by which genetic variation affects cellular pathways, brain networks and ultimately behavior is largely unknown," Rudie said. "We wanted to know how this risk allele may affect brain circuitry, predispose an individual to ASD and exacerbate these social deficits." -- *Mark Wheeler, UCLA Newsroom*

For more see: http://newsroom.ucla.edu/portal/ucla/study-reveals-how-a-common-gene-238437.aspx

Welcome Interdepartmental Graduate Program in Neuroscience Students

Please join the BRI in welcoming the incoming class of 2012.

Erica Arroyo received a Bachelor of Science in Biochemistry and Biology from Arizona State University.
Research interest: The potential synaptic errors that occur during cortical development of a disease model of Fragile X Syndrome.
Fun fact: Erica has lived in Texas, New Mexico, Florida, Arizona, Virginia and California.

Shivan Bonanno received a Bachelor of Arts in Molecular and Cell Biology – Neurobiology from U.C .Berkeley.
Research interest: Neural computations and modulation in circuits mediating behavior.
Fun fact: Shivan loves to play and learn about new types of music.

Danial Cantu received a Bachelor of Science in Biology from U.C. Irvine.

Michael Einstein received a Bachelor of Arts in Biology from Carleton College.
Research interest: The physiology of circuits responsible for behavior.
Fun fact: Michael listens to and plays a good deal of music.

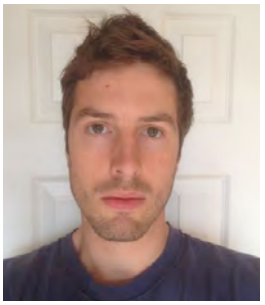
Joel Frolich received a Bachelor of Science in Neuroscience from The College of William and Mary.
Research interest: Utilizing neuroimaging methods and connectivity analysis to study neuropsychiatric diseases such as schizophrenia.
Fun fact: Joel is interested in philosophy of mind and the nature of consciousness.

Nick Hardy received a Bachelors of Science in Psychology from the University of Maryland College Park .
Research interest: Neural networks and neural computation.
Fun fact: Nick studied abroad in China while at college and while there sampled fried scorpion, seahorse, chicken feet, and pig tongue (not all at once). "Yummy!" he says.

Leanna Hernandez received a Bachelor of Arts in Psychology from the University of Southern California.
Research interest: The study of brain development in typically developing children and children with autism spectrum disorders, with the goal to integrate genetic information, neuroimaging phenotypes, and behavioral measures of social and emotional cognition.
Fun fact: Leanna is a horseshoes champion.

Garret Matthew received a Bachelor of Science in Molecular Biophysics and Biochemistry from Yale University.
Research interest: Brain cancer.
Fun fact: Garret's brother (a bank teller) recently thwarted a bank robbery. "A guy in a ski mask put a note on the desk facedown. My brother said he wasn't allowed to read hand-written notes (not true). He has no fear," Garret said.

Daniel Nachun received a Bachelor of Arts in Biology with concentrations in Neuroscience and Biochemistry from Williams College.
Research interest: Drug addiction and the opiate system.
Fun Fact: Daniel hails from Nebraska.



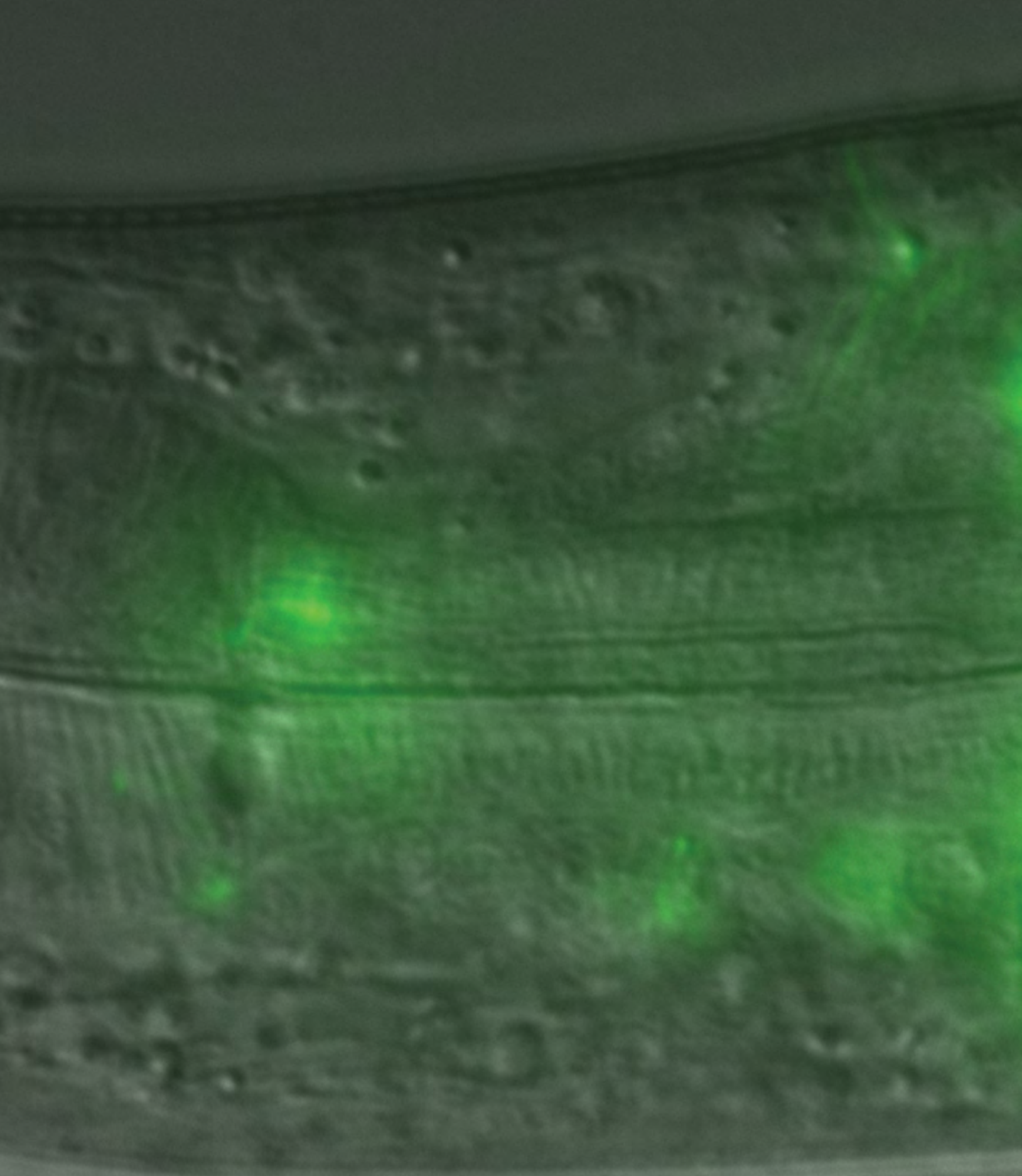
Andrew B. O'Keeffe received a Bachelor of Medicine and Bachelor of Surgery from the University of Oxford.
Research interest: Deep brain stimulation and brain-machine interfaces.
Fun fact: Andrew is a fully qualified rescue diver, and also enjoys judo and surfing.

Andrew Segal received a Bachelor of Science in Neuroscience from UCLA.
Research interest: Neural development through molecular and genetic perspectives.
Fun fact: Andrew enjoys sailing and home brewing.

Alice Zhang received a Bachelor of Arts in Molecular Biology from Princeton University.
Research interest: Function, evolution, and regulation of biological networks, and their dysregulation in human disease states.
Fun fact: Alice once competed in a Miss Teen USA pageant.

Good luck to everyone in the coming years, and welcome to the neuroscience community at UCLA.

Cover Image: Detail of a *C. elegans* larva expressing green fluorescent protein (GFP) in a subset of sensory neurons. Image provided by Dr. Elissa Hallem.



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