

# Partners *in* Discovery

# PARKINSON'S INTERRUPTED?

## **UCLA Researchers Find Molecular “Tweezer” Drug Shows Promise in Stopping Parkinson's Progression**

Parkinson's disease (PD), suffered by more than 500,000 people in the United States alone, is a disorder of the central nervous system that affects movement and worsens over time. As the Baby Boomers age, it is estimated that the number of people with the disease will rise accordingly. Yet, despite several effective therapies to treat the symptoms of Parkinson's, nothing slows its progression. Enter UCLA's Movement Disorders Program, under the direction of Jeff Bronstein, M.D., Ph.D.

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## Chair's Column



John C. Mazziotta, M.D., Ph.D.  
Chair, Department of Neurology  
Stark Professor of Neurology  
David Geffen School of Medicine at UCLA

"We look toward working together to harness an engine of success and drive basic science and clinical research."

Neurodegenerative diseases are disorders that, for currently unknown reasons, cause nerve cells to die. Patients exhibit neurological symptoms, once the capacity for the brain and spinal cord to mask the effects of this attrition is exhausted. For each of these neurodegenerative diseases, the signs and symptoms differ based primarily on the types and locations of the cells that are damaged by the disease process. In Alzheimer's disease, the outer cortex of the brain and regions that subserve memory and cognition are maximally affected, resulting in memory disorders and cognitive decline. In Parkinson's disease, brain networks that control posture, movement and the initiation of movement are the primary targets and patients develop tremors, slowed movements and a characteristic stooped posture. In Huntington's disease, regions of the brain that control movement and thinking are primarily affected with patients developing involuntary movements, memory disorders and psychiatric symptoms. In ALS (Lou Gehrig's disease) the motor system of the brain is the target of the degeneration resulting in weakness, muscle twitching and paralysis.

All of these disorders have a common theme, abnormally folded proteins accumulate in specific regions of the brain. These locations vary by disease. The collections of folded proteins or the process that leads to their accumulation results in disturbances in the cells and, ultimately, to cell death. While the diseases appear quite distinct clinically, the common process of protein accumulation actually makes them more related than was once thought.

In the UCLA Department of Neurology, we have clinicians and scientists who study all of these diseases in the clinic and in the laboratory. The exchange of information and the insights obtained in one disorder facilitates and accelerates understanding of the other neurodegenerative disorders. By viewing these diseases as different end points of a common mechanistic continuum, it may be possible to greatly accelerate insights into the causes of these disorders and strategies for interfering with the abnormal process leading to new treatments and, ultimately, cures.

Considering the neurodegenerative disorders as a collection of diseases that should be studied in common rather than in isolation, we at UCLA have a distinct advantage and opportunity that would not be realized at smaller institutions where only one disease might have a significant research and clinical commitment.

It is our intent to work collectively to understand these disorders and find effective treatments for them. With you as our partners in this process, we feel confident that we can achieve results at UCLA that will inform our colleagues internationally and move forward the important process of solving some of medicine's most difficult and costly disorders.



### Art of the Brain Celebrates 13th Annual Gala, "The Art of Singing and Speaking for Joy"



Master of Ceremonies Jason Barry (left), general assignment reporter for KPHO-TV (CBS) in Phoenix, Arizona, with Art of the Brain founder, writer and artist, Judi Kaufman (center) and UCLA Neurology's Dr. Timothy Cloughesy (right) on October 6, 2012 at the 13th Annual Art of the Brain Gala at UCLA Schoenberg Hall. The event, which raises money and builds public awareness for the UCLA Neuro-Oncology program, featured the Gay Men's Chorus of Los Angeles; L.A.-based indie pop band Brandy Loves Alexander; and local hip hop artist Tulgat Vandandorj, along with showcasing the cuisine of local eateries, many of which donated food for the evening. Art of the Brain spotlights the talent, strength, and courage of brain cancer patients.

"Not only are we working on behalf of donors, but we're also trying to be good stewards of our community.

- Janice Fong Wolf

## Honoring a Donor's Wishes:

San Luis Obispo County Community Foundation Selects UCLA's Mary S. Easton Center for Alzheimer's Research as A Beneficiary of A Local Estate



Burt Polin (Photo courtesy of The Tribune, San Luis Obispo)

Virginia and Burt Polin were married for nearly 70 years. A San Luis Obispo native and lifelong resident, Burt was a dry land wheat rancher for more than 40 years, on Carrizo Plains land he inherited from his grandfather. He was also a shrewd real estate investor and broker, opening Polin-Truchan Realty in 1964. Active in the local community, Burt was a member of the Elks Club and the Caballeros and Virginia sang in many choir groups. The couple left a sizeable estate, thoughtfully administered by the San Luis Obispo County Community Foundation, which selected UCLA's Mary S. Easton Center for Alzheimer's Research as the beneficiary of a \$250,000 bequest.

According to Janice Fong Wolf, the foundation's director of grants and programs, the Burt W. and Virginia Polin Charitable Fund was set up in 2007. At that time, Virginia Polin worked with the former executive director and an estate attorney to identify areas, including more than 30 organizations—many of them local—to benefit from the fund upon her death.

Virginia passed away in 2010, and the foundation's real work began. The Burt W. and Virginia Polin Charitable Fund is carrying on the couple's legacy of commitment, thanks to

the diligence of the San Luis Obispo Community Foundation. "We really strive to honor the donor's wishes," Fong Wolf said. "Not only are we working on behalf of donors, but we're also trying to be good stewards of our community. In this case, our direction was to select the charitable organization on behalf of Mrs. Polin."

She explained that the grants and distribution committee researched and identified institutions online and requested materials. The committee reviewed them to determine which they thought would be most appropriate. The Mary S. Easton Center for Alzheimer's Research made a positive impression, which was confirmed by the extensive information that senior director of development Patricia Roderick submitted for review.

"We did a lot of reading and had many discussions over several months," Fong Wolf said. "It was important to know what was going on beyond our borders. We were looking for institutions that do cutting-edge, innovative research on a high level and we had to make a conscious choice about which organizations to select—from among HIV, stem cell, Parkinson's disease, and Alzheimer's disease. Many of these



Above: Barry VanderKelen, Executive Director, San Luis Obispo County Community Foundation, and Janice Fong Wolf, Director Grants & Programs




Left: Virginia Polin (Photo courtesy of The Tribune, San Luis Obispo)

were organizations outside of our region, not previously familiar with the Polins."

The Easton Center is deeply grateful for the careful stewardship executed by the San Luis Obispo County Community Foundation.





“The zebrafish allows us to test the drug quickly and is a model that allows us to gain an understanding of how the drug works,”

According to Bronstein, the question becomes, “Can we stop abnormal aggregation and thus stop Parkinson’s?” The answer may well be yes. Bronstein has been collaborating with UCLA associate professor of neurology Gal Bitan, Ph.D., who discovered a novel compound known as a “molecular tweezer,” which can interfere with protein aggregation. Bronstein and Bitan, along with their colleagues, recently reported that in a living animal model, CLR101 blocked a-synuclein aggregates from forming, stopped the aggregates’ toxicity, and, more important, reversed aggregates that had already formed in the brain. What’s more, the “tweezer” accomplished this without interfering with normal brain function. The UCLA scientists recently published the results of their study in the journal *Neurotherapeutics*.

Molecular tweezers are complex molecular compounds that are 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 had been working with the particular molecular tweezer CLR01 for some time, and he felt it could be applied to Parkinson’s. Working first in cell cultures, researchers found that CLR01 was able to accomplish its mission.

“The most surprising aspect of the work,” Bronstein says, “is that despite the ability of the compound to bind to many proteins, it did not show toxicity or side effects to normal, functioning brain cells.” Process specific, the compound attached only to the targeted aggregates.

The researchers next focused on a living animal, the zebrafish, a tropical freshwater fish commonly found in aquariums. The zebrafish model developed in the Bronstein Lab is important, since zebrafish are vertebrates and share most of the same brain regions as humans, are easily manipulated genetically, develop rapidly, and are transparent, making it feasible to measure their biological processes in living fish.

Using a transgenic zebrafish model of Parkinson’s disease, the researchers added CLR01 and used fluorescent proteins to track the tweezer’s effect on the aggregations. They found that, just as in cell cultures, CLR01 prevented a-synuclein aggregation and neuronal death, thus stopping the progression of the disorder in the living animal model and greatly mitigating toxicity.

Continued  
from Cover

“The goal of the UCLA Movement Disorders Program is to improve the quality of life for people with Parkinson’s disease and other movement disorders,” says Dr. Bronstein. “Our secondary goal is to do everything we can with established treatments. We provide comprehensive and holistic care, taking the entire patient into account. Long-term, we hope to develop new potential therapies and ultimately stop the progression of the disease, but first we need to develop these therapies in basic science labs, and then create a strong clinical trial center to test new treatments.” Bronstein explains that the program concurrently utilizes parallel teams of scientists in order to achieve the goals.

While the exact cause of PD is unknown, evidence from studying its underlying molecular basis points to a protein called alpha-synuclein, or a-synuclein. Bound together in “clumps,” or aggregates, a-synuclein has been found to be common to all patients with Parkinson’s. The aggregates in this common pathway become toxic and kill neurons in the brain.



"The zebrafish allows us to test the drug quickly and is a model that allows us to gain an understanding of how the drug works," Bronstein explains. "We learned that 1.) aggregation is toxic and, 2.) it blocks its own breakdown. The tweezer not only breaks the aggregation, but also reverses downstream progression of the disease."

Dr. Bitan is leading the studies testing CLR01 in other scientific models. "We are doing all the prep work to make sure the dosage is safe before we take it to clinical trials," Bronstein says.

There are currently more than 30 diseases with no cure that are caused by protein aggregation and the resulting toxicity to the brain or other organs, including Parkinson's, Alzheimer's and Type 2 diabetes. It is therefore critical, Bronstein says, to find a way to stop the aggregation process. Over the last 20 years, researchers and pharmaceutical companies have attempted to develop drugs to prevent abnormal protein aggregation, but so far, they have had little or no success.

According to Bronstein, the complication is in finding a therapy that targets only the aggregates. "In Parkinson's, for example, a-synuclein is naturally present throughout the brain. The trick, then, is to prevent the a-synuclein protein aggregates and their toxicity without destroying a-synuclein's normal function, along with, of course, other healthy areas of the brain."

He notes that it is very expensive to take a drug to market. "There are some promising drugs, but we still need to prove that they are safe and whether they actually work. The good news is that we are developing biomarkers that will enable us to test drugs faster and in fewer people."

"To that end, we are also working on repositioning drugs that already exist for other purposes," Bronstein states. For example, a class of medications used to treat high blood pressure is currently showing promise in slowing the progression of Parkinson's disease. A collaborator of Dr. Bronstein, Dr. Beate Ritz, recently found that some of these blood pressure medications are associated with a lower risk of getting Parkinson's disease, and studies in the Bronstein lab suggest that they can help stimulate the breakdown of a-synuclein aggregates.

## Maximizing Quality of Life for PD Patients and their Families:

Sometimes, in selected cases of advanced Parkinson's disease, surgery can be the best treatment option. Dr. Jeff Bronstein was the Southern California Principle Investigator of a large national study funded by the Veterans Administration and NIH to study a procedure called deep brain stimulation (DBS). The first question asked in the study was, "Is DBS better than best medical therapy?" The answer, published in 2010 in the *Journal of the American Medical Association*, was yes. Next, the study investigated the advantages and disadvantages of placing the electrode in two different areas of the brain: the subthalamic nucleus (STN) or globus pallidus interna (GPI). They found that both sites offer significant and equal benefits in motor function; but, surprisingly, GPI DBS showed some advantages in non-motor function over STN DBS. These results, from the largest surgical trial in PD ever performed, were published in a 2011 article in the *New England Journal of Medicine* and are already changing surgical practices throughout the world.

Take the case of Jim Sweet, reported in *People* magazine on September 4, 2006. Sweet, a happily married, church-going father of two, was diagnosed with Parkinson's disease in 1998. In two years, he turned into a compulsive gambler who racked up \$150,000 in debt and a Las Vegas arrest. Acting on a hunch, Dr. Bronstein took him off of the drug that was helping to steady his hands and, almost immediately, Sweet's gambling urges ceased. Unfortunately, over time Mr. Sweet developed fluctuations in his condition which were no longer manageable with medications alone. He then turned to DBS to help treat many of these problems. As of this writing, Mr. Sweet was scheduled for his first programming after DBS surgery. While it can take months of programming to reach optimal results, Mr. Sweet is already seeing some benefits.

"Jim Sweet's case serves as an example of how we use a well-established technique to refine and improve outcomes," says Bronstein. "We study cases like this in the Movement Disorders Program, and we make primary care physicians and neurologists aware of them so that they can help maximize the quality of life for their patients and their patients' families. A case like this also provides a clear example of why a drug to halt or even slow the progression of PD is so important, and why clinical trials are so critical."

UCLA's Deep Brain Stimulation Program is coordinated by **Yvette Bordelon, M.D., Ph.D.** and neurosurgeon **Nader Pouratian, M.D., Ph.D.** Dr. Bordelon also is working on non-invasive imaging studies in order to measure aggregates in humans. She is investigating the use of a specific brain-imaging technique, known as PET scan, to measure the clumping of the proteins that occurs in the brains of people with PD and other neurological disorders, and she believes that the development of biomarkers is a crucial step in finding new treatments that can actually slow the course of PD.

# OUT OF THE SHADOWS

**UCLA Seizure Disorders Center  
Takes Lead In Bringing Epilepsy  
to the Forefront**

**Jerome Engel, Jr.,  
M.D., Ph.D.**

Director, UCLA Seizure  
Disorder Center  
Professor of Neurology,  
Neurobiology, and Psychiatry  
and Biobehavioral Sciences  
Jonathan Sinay Distinguished  
Chair,  
David Geffen School of  
Medicine at UCLA.

Epilepsy affects nearly 3 million Americans and 60 million people worldwide; the health burden caused by the disease is equivalent to that of lung cancer in men and breast cancer in women. Epilepsy is considered one of the most common serious disorders of the brain. Although most seizures can be controlled by medication, one third of Americans with epilepsy will continue to suffer from seizures despite attempts to control them through the use of drug treatment. Less than 1% of the 1-million people in the U.S. with drug-resistant epilepsy are referred to epilepsy centers, where specialized diagnosis and treatment are available.

Dr. Jerome Engel, Jr. tirelessly devotes his time to research, patient care, and teaching the next generation of medical students – having written and edited the texts that are the gold standard in medical schools across the globe. Epilepsy, one of the most serious health burdens worldwide, is only now emerging from the shadows. Since joining UCLA in 1976, Dr. Engel's contributions to the medical field have inspired researchers and future medical professionals, in addition to providing hope to patients who face numerous challenges every day.

UCLA faculty members have participated in recent national and international efforts to raise consciousness about epilepsy and have conducted ground-breaking research to elucidate the disorder's fundamental mechanisms in order to improve the diagnosis and treatment of epileptic seizures.

The search for reliable biomarkers has become a primary goal for epilepsy, in addition to other areas of medicine. Reliable biomarkers are essential for the cost-effective discovery and validation of drugs and other interventions designed to prevent, treat, and cure epilepsy. Such biomarkers will also revolutionize clinical care by eliminating the trial-

and-error approach now used to find appropriate drugs for individual patients.

Recently, UCLA scientists identified pathological high-frequency oscillations (pHFOs), which appear to represent the fundamental neuronal abnormalities underlying certain chronic epilepsy conditions—in particular, mesial temporal lobe epilepsy (MTLE), the most common form of epilepsy in adults, and the most drug-resistant. Not only do pHFOs provided important insights for understanding basic defects that could become targets for novel approaches to treat and perhaps prevent or cure epilepsy, but also pHFOs are now the most likely candidates for biomarkers of epileptogenesis (the development and progression of epilepsy) and epileptogenicity (the presence and severity of an epilepsy condition). Once antiepileptogenic interventions are available, biomarkers would permit identification of at-risk patients for preventive treatment before epileptic seizures occur. UCLA scientists are currently very close to using pHFOs as biomarkers to identify the epileptogenic region that needs to be removed in patients who are surgical candidates, which could eliminate the need for other time-



consuming and expensive presurgical evaluations. Advancing the diagnosis of epilepsy has been a major objective of the UCLA epilepsy clinical program. EEG telemetry, the mainstay of inpatient diagnosis for all epilepsy centers worldwide, was developed at UCLA based on collaboration of UCLA scientists with the National Aeronautic and Space Administration to record EEGs from chimpanzees orbiting in space.

The first PET scans for epilepsy were also performed at UCLA, and the University continues to be a leader in the field of modern neuroimaging, as well as clinical neurophysiology, as applied to epilepsy. UCLA has one of the most advanced neuroimaging laboratories in the world, and collaboration with the Seizure Disorder Center is resulting in novel approaches using magnetic resonance imaging (MRI) to visualize not only the structural and functional aberrations associated with the epileptogenic brain region, but also its relationship with other areas of the brain. A new field of study called connectomics, utilizes these approaches along with computational modeling, to understand how widely spaced areas throughout the brain work together to generate normal and also abnormal behaviors. UCLA scientists are leading the way in demonstrating how the abnormalities responsible for the generation of spontaneous epileptic seizures requires the participation of large areas of the brain, and are among the first to apply this exciting new area of connectomics to understand epilepsy at the level of the whole brain. The results of this research will not only have a profound impact on diagnosis, but it will also suggest novel approaches to treatment.

A major focus of the UCLA Seizure Disorder Center clinical program has been on surgical treatment of epilepsy. UCLA is recognized as one of the leading epilepsy surgery centers in the world, as a result of its many contributions to improved approaches toward presurgical evaluation and surgical treatment.

Those who are referred for surgery and receive it, have an average delay between onset of epilepsy and surgery of over 20 years. During this time, patients experience prolonged mental and emotional trauma, without gaining the interpersonal and vocational skills necessary to live on their own. Although no longer burdened by seizures, too many remain dependent on their families and society.

The results of UCLA's landmark multicenter Early Randomized Surgical Epilepsy Trial (ERSET) funded by the National Institutes of Health, were published in the *Journal of the American Medical Association (JAMA)* in March 2012. This is only the second randomized trial of epilepsy surgery to be published, and the first to study patients shortly after failure of two antiepileptic drug trials, and to randomize patients after presurgical evaluation. Results of the study revealed that 85% of patients who underwent early surgery were seizure free, as compared with none of those who continued on medication. It is greatly hoped that publication of the ERSET study in the prestigious journal *JAMA* will stimulate earlier referral of patients with refractory seizures to epilepsy centers to correct this unfortunate situation.

## Meet Our Fellows

### Mateo Calderon-Arnulphi, M.D.



Mateo Calderon-Arnulphi, a Fellow in Stroke Neurology, believes that UCLA Neurology is the place to be—especially for a stroke neurologist. “This is the place for innovation, under Dr. Jeffrey Saver and Dr. David Liebeskind. At UCLA, we see all demographics: the VA is for the military; Olive View is for the underserved; UCLA Westwood is a referral center for complicated cases from all over the world. It is a mecca for teaching and learning, and it’s all in synch.”

It was a vascular surgery fellowship that inspired Dr. Calderon-Arnulphi to become a neurologist. A native of Argentina, Calderon-Arnulphi followed his mother, a physicist at the University of Illinois, to that state, where he spent three years working in a physics lab learning a laser technique to measure the amount of oxygen in the brain during surgery. He then worked in neurosurgery at the University of Illinois Medical Center in Chicago, where he developed algorithms to determine when brain tissue is at risk for stroke. Currently, he is working on a non-invasive laser helmet for use in emergency vehicles to measure brain oxygenation in possible stroke victims.

More than the technology, though, Dr. Calderon-Arnulphi appreciates the human aspect of medicine. “I value the patients the most, and I love mentoring the students,” he says. “I participate in a premed program led by Dr. Sidney Starkman. Every other week we have lunch with a group of premed students and talk about all aspects of medicine. They ask questions about how we can become better doctors. I believe it is by expanding patient interactions. There is no test that should come between a patient and his doctor.”

Dr. Calderon-Arnulphi learned from his own mentor that you will never be wrong if you put the patient first. “I have had tremendous mentors. Neuroscience is complicated and I have been blessed in finding the right mentors. You pass on the information, doctor to doctor, generation to generation, and no textbook can teach you that. To train that person is our mission.”

It is clear that Mateo Calderon-Arnulphi is passionate about his chosen specialty. “I moved from the other side of the world to do this,” he says.

## The Power of Philanthropy



Richard N. Merkin, M.D.

*"Some people wait until the end of their lives to become philanthropic, but I've been doing this most of my adult life."*

# Richard N. Merkin, M.D.

Dr. Richard Merkin is a visionary healthcare expert who is committed to supporting academic research. As founder, president, and CEO of Heritage Provider Network, he develops clinically focused networks designed for the managed care environment, bringing efficient and quality-driven systems to the communities in which the company operates.

Dr. Merkin has a long-standing interest in both prevention and cure. He is co-founder of FasterCures, an action tank that seeks to decrease the time it takes to bring important new medications from bench to bedside. To that end, he founded the Heritage Medical Research Institute, a nonprofit medical research corporation emphasizing healthcare quality and outcome studies. Responding to the nation's \$2-trillion healthcare crisis, Dr. Merkin created, developed, and sponsored the \$3-million Heritage Health Prize for predictive modeling to save more than \$30 billion in avoidable hospitalizations. "If we can prevent these avoidable issues, then we can reallocate funds and go from care dollars to cure dollars," he says.

Dr. Merkin's philanthropic commitments run deep. He established the Richard Merkin Foundation for Neural Regeneration at UCLA, as well as the Richard Merkin Foundation for stem cell research at the Broad Institute at Harvard, and the Richard Merkin Initiative at the Johns Hopkins Brain Sciences Institute. In addition, he endowed two scholars at the Engelberg Center for Health Care Reform at the Brookings Institute to study payment reform and clinical leadership, and funded the Brain and Health Innovation Program at the Zilkha Neurogenetic Institute at the Keck School of Medicine.

His interest in philanthropy began in his 20s, when he did volunteer work and participated in philanthropic missions. "Some people wait until the end of their lives to become philanthropic," he says, "but I've been doing this most of my adult life."

The Richard Merkin Foundation for Neural Regeneration at UCLA will help Drs. Bruce Dobkin, S. Thomas Carmichael and others with their research endeavors. "There is a lot of money being spent on cancer research, but not as much on the brain, spinal cord, and peripheral nervous system, so it seemed that would be a good place," Dr. Merkin explains.

Dr. Merkin is passionate about his belief in innovation and challenge. "Some of the younger physician scientists have difficulty getting grants because their ideas aren't proven," he says. "What is a radical breakthrough today was a crazy idea yesterday. We need to fund those crazy ideas, because it's the young people who need that funding." Enter Dr. Merkin's 3-3-3 program. Up to three people can team up to come up with an idea. They get \$3,000 and three weeks in which to do it. "Maybe one in 20 will be successful. If your idea isn't successful, we applaud you anyway. We do it to encourage innovation in order to improve the system."

"The UCAs are the gems and jewels in the system and we all have to come together to make it more efficient," he says.

Clearly, Dr. Richard Merkin is someone who, in the truest sense, uses philanthropy to improve healthcare.



## Volunteer Faculty

## Cyrus K. Mody, M.D., M.S.P.H.

Every October since 1989, Cyrus Mody has been shutting down his busy private practice in Neurology and Clinical Neurophysiology in order to run the consult service at Harbor-UCLA Medical Center, teaching Neurology to residents and medical students three days a week. He also helps train Cedars-Sinai/UCLA Neurophysiology Fellows every Monday by reading the day's EEGs and Evoked Potentials with them. It is his way of giving back—in exchange for what he believes was a truly excellent education, thanks to his own mentors.

"I thought teaching would be a good way to give back," he says, noting that he gains more than he gives. "I learn different points of view and I get a different perspective. The days are long that month, but it's worth it."

Dr. Mody, who completed his residency in Neurology at Harbor-UCLA Medical Center, was the first Neurophysiology Fellow trained by Drs. Hugh McIntyre and Thomas Anderson from 1986-1987, and the first Neurobehavior/Neurophysiology Fellow trained by Drs. McIntyre and Bruce L. Miller from 1987-1988. He specializes in the physiology of the brain, spinal cord, nerves, and muscles, as well as electrical testing—including Electroencephalography (EEG), which monitors brain activity through the skull, and Electromyography (EMG), which is used to diagnose nerve and muscle dysfunction, and evoked potentials used to evaluate spinal cord disease. He is also one of the pioneers in the specialized field of topographic brain mapping using EEG.

When he is teaching, though, Dr. Mody starts with the basic art of history-taking, and performing a thorough neurological examination in order to make an accurate diagnosis. "It's a drill about doing things the right way. The students enjoy it."

Dr. Mody is a recipient of UCLA Neurology Voluntary Faculty Awards for Excellence in Teaching in 2005 and 2010, and the Harbor-UCLA Medical Center Voluntary Faculty of the Year Award for Excellence in Teaching in 2010.

"By doing this, I am also able to bring the private practice world to students and residents—it gives the residents an idea of what real-world neurology looks like. It makes them more well-rounded to know how neurology is practiced in both an academic and private-practice setting," he explains. "For me, it's the right thing to do. It's very fulfilling."

Dr. Mody and his wife, who is Chief of Cardiology at the Greater Los Angeles VA, also teach in Japan almost every year.

## Why I Do This



## Liana Apostolova, M.D.

Associate Professor of Neurology,  
Director, Easton Neuroimaging Laboratory at the Mary S.  
Easton Center for Alzheimer's Disease Research at UCLA.

"Neurology is a calling. You don't choose it. It chooses you," says UCLA's Dr. Liana Apostolova, who conducts clinical and neuroimaging research in Alzheimer's disease, mild cognitive impairment, and other neurodegenerative disorders. Her main research focus is the development and validation of structural

imaging biomarkers in Alzheimer's disease and mild cognitive impairment, both from an epidemiological and a pharmacotherapeutic perspective. This important research dimension coincides with the increased interest in disease-associated biomarkers that will allow physicians to diagnose and treat dementia as early as possible. Dr. Apostolova also studies the brain-behavior correlations in Alzheimer's disease, Parkinson's disease, and other dementias.

Although Dr. Apostolova came to UCLA for a Fellowship in Dementia and Biobehavioral Neurology in 2005, her career-path in academic medicine began generations ago in Bulgaria. "I come from a long line of academics and physicians," she explains. "My great-grandfather was an officer in the Tsar's court in Bulgaria; my great-grandmother spoke nine languages and was a teacher. She was tuning-in to language lessons on TV before she died at 90. My grandmother was a dentist, my grandfather a physiology professor and M.D. who spent time in research. My dad was a professor of leather chemistry at Technical University of Sofia, and my mom, who had a passion for research and wanted to become a biochemist, spent the last 15 years of her career as a professor of biochemistry at Northwestern University in Illinois."

A summa-cum-laude graduate of Medical University in Sofia, Dr. Apostolova did her internship at Ravenswood Hospital in Chicago, followed by a residency in neurology at University of Iowa Hospitals and Clinics. That is where she studied cognitive neurology and became inspired by her first neurological experience. "It takes intelligence, and it's stimulating. You drill into the patient's history without any technology. Neurology is not like any other field. We still don't know anything about the brain, which is fascinating," she says.

Iowa is also where she got involved with neuroimaging. "If you're good with scans, the amount of information you can get from the scan can enable you to really fine-tune the results."

Dr. Apostolova believes that cognitive neurology is the area we don't really understand. How does the child become cognitively aware? Why does the brain malfunction? "I meet patients and I love them and wish I could select from 10,000 drugs to treat them. It's the research I do that balances it. Fortunately, we are finding biomarkers of Alzheimer's disease presence and progression—if only we can find it early enough to do something for the people at high risk of developing it."

The research is laboratory-intensive and takes a lot of time. Currently, Dr. Apostolova has five full-time research assistants in her lab, plus undergrads and graduate students as rotating scholars.

A self-described workaholic, she takes time to have fun with her friends and family—sons Julian, 10, and Martin, 5, and husband Val, who is a network administrator.

## You Can Make A Difference!

The Department of Neurology at the David Geffen School of Medicine at UCLA is an academic department dedicated to understanding the human nervous system and to improving the lives of people with neurological diseases.

The Department of Neurology has many pressing needs to continue our mission. You can direct your charitable gifts of cash, securities, real estate, art, or other tangibles to our greatest needs, under the direction of Dr. John Mazziotta, Chair of the Department, or to specific research, training, laboratories, or programs of specific physicians or diseases. For more information please contact Patricia Roderick, Senior Director of Development, UCLA Department of Neurology, (310) 267-1837 or [proderick@support.ucla.edu](mailto:proderick@support.ucla.edu).



MEET  
A  
SCIENTIST

# Mayank R. Mehta, Ph.D.

*Professor of Neurophysics*

The human brain controls all aspects of behavior including perception, memory, learning, thought, breathing, sleep, etc. It comprises 100 billion neurons, with a language all their own that manifests as electrochemical impulses.

It is with these impulses that these billions of neurons communicate with each other and control behavior. The key question is: what is the language of the neurons?

UCLA researcher and professor of Physics and Neurology Mayank Mehta studies neuronal language in hopes of unlocking the memory loss mysteries associated with Alzheimer's disease, stroke, and epilepsy. "The challenge is to figure out how the brain communicates with itself and how it turns that communication into behavior," he says.

Neurophysics has allowed Mehta to develop a technique at UCLA that enables his team to pick up the activity about hundred single neurons at the same time during natural behaviors such as spatial exploration and even sleep, and determine the changes in their activity over months.

Using rodents as subjects, Mehta and his team studied the hippocampus, neocortex, and entorhinal cortex, all of which are important for learning and memory. "We created a virtual reality for rodents in a laboratory setting," he says. "It is not harmful or invasive. They wear a sleeveless t-shirt that is held in place by Velcro. They walk on a ball, immersed in a virtual reality that we can control and change. We can manipulate space and events around them, teleport them to distant places and figure out how their brains learn the structure of space."

"Unlike us, millions of neurons talk all at once, often using different rhythms, which

makes their language very strange and difficult to understand" he explains. "The good news is that we can change the connections between neurons. These connections, called synapses, are modified by activity and vice versa. So, one of our goals is to understand how the synaptic changes govern neural language."

Another mystery is: what does our brain do while we are asleep? "During the one-third of our lives that we are sleeping, the brain is still active very active. Further, we recently discovered that different parts of the brain talk to each other using distinct rhythms during sleep and this intra-brain dialogue is critical for learning and memory."

Mehta's lab has developed hardware to 1) Measure and manipulate neuronal activity and behavior; and 2) Measure the activity of ensembles of well-isolated neurons from many hippocampal and neocortical areas simultaneously during learning and during sleep. In addition, they have developed data analysis tools to decipher the patterns of neural activity and field potentials, and their relationship to behavior. Currently, they are developing biophysical theories of synapses, neurons, and neuronal networks that can explain the experimental findings, relate them to the underlying cellular mechanisms, and make experimentally testable predictions. It is hoped that the results will point to novel ways of treating learning and memory disorders.





## Luncheon Honors Former Beverly Hills Mayor and Wife, Raises Funds to Fight Parkinson's Disease

Arik Johnson, Psy.D. ( Fenton Family Clinical Coordinator at UCLA), The Honorable William Brien, M.D. ( Mayor of Beverly Hills), Mrs. Judie Fenton ( Honoree), Jeff Bronstein M.D., Ph.D. ( Director Movement Disorders Program and Professor of Neurology at UCLA) at the "Spirit of Giving" luncheon organized by members of the Beverly Hills Active Adult Club (BHAAC). The lunch and boutique event honored former Beverly Hills Mayor Frank Fenton and his wife, Judie Fenton. Proceeds from the event were split between the UCLA Movement Disorders Program and the BHAAC. The Fenton family helped fund a new position in the Department of Neurology to assist patients and families dealing with the psychological effects of Parkinson's disease.



## UCLA Movement Disorders Program Honors Donor Heinrich Kolbel

Longtime UCLA donor Heinrich Kolbel (left) shakes hands with UCLA Movement Disorders Program Director Dr. Jeff Bronstein after the unveiling of a plaque commemorating his generous support for Parkinson's disease research. Dr. Kolbel, who had been a 31-year employee of the University, was motivated to donate when he witnessed the disruption and devastation Parkinson's caused to a friend. He chose UCLA charitable gift annuities as the best way to help fulfill his philanthropic goals. His gift is in honor of William Johns.



## Students Zumba Away for UCLA

Stacie Labrozzi, a teacher at John Handley High School in Winchester, Virginia, and her family are dedicated to raising money to support Retinal Vasculopathy with Cerebral Leukodystrophy research. She organized students from the Interact and Key Clubs to hold two fundraisers, including a Zumbathon (pictured) and Hat Days. These events attracted over 100 students, and proceeds advance the work of UCLA physician researcher Joanna Jen, M.D., Ph.D. Thanks to Stacie, Debra Simon, Megan Hamm, and the students for their support.

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## Norman S. Namerow, M.D.

Life Through a Lens: Submarines  
to the Huli People of New Guinea

UCLA Neurology alumnus Dr. Norman S. Namerow is a physician with many interests and many accomplishments. The esteemed neurologist counts opera, art, and exotic travel among his passions, and he has been lucky enough to be able to combine them.

His enduring love of opera has led him to travel all over the world to hear favorite singers, as well as to amass a collection of more than 1,000 CDs. His love of travel—especially adventure travel—has led him to exotic locations, including Africa, New Guinea, Sumatra, and Borneo, all captured through his passion for photography. On the more civilized side, Dr. Namerow and his wife of 41 years, Barbara, are avid collectors of 19th century Victorian art, two pieces of which they donated to the Getty Museum, where they are on permanent display.

Dr. Namerow attended the UCLA School of Medicine from 1954-1958. He did his internship and a year of ophthalmology residency at UCLA, followed by a neurology residency. He joined the UCLA faculty in 1969 as an assistant professor, becoming a full professor in 1971.

Dr. Namerow's initial neurological research was a multicenter study using adrenocorticotrophic hormone (ACTH) as a treatment for Multiple Sclerosis (MS)—a contributing study that opened the door for the use of steroids to treat MS. After sending his MS patients to physical therapy, Dr. Namerow became interested in neurological rehabilitation and was approached by Daniel Freeman Memorial Hospital, which built a 58-bed unit devoted to rehab, the Center for Diagnostic and Rehabilitation Medicine.

While at Daniel Freeman, Dr. Namerow started a pioneering, multidisciplinary pain

management program that he directed for 25 years. "We had amazing success at getting people off drugs and improving their quality of life. Sherm Mellinkoff (former UCLA Medical School Dean Sherman D. Mellinkoff) made us an affiliate of UCLA and our group trained many medicine residents in neurology over the 27 years we were there," he says. When he retired from Daniel Freeman in 1999, they renamed the rehabilitation wing the Norman S. Namerow, M.D., Rehabilitation Unit.

Dr. Namerow was the primary advocate for multidisciplinary care of patients with chronic pain and neurological injury and he actively lobbied with two colleagues within the American Academy of Neurology for additional support for this type of care. Their efforts led to the creation of the American Academy of Neurology Section on Neurorehabilitation in 1985, and eventually to the creation of the American Society of Neurorehabilitation (ASNR) in 1990. Dr. Namerow became its first president, playing a significant role in the Society's development.

President of the UCLA Medical Alumni Association (MAA) from 1999 – 2002, Dr. Namerow continues to serve that organization as an associate Board member. He also has served on the admissions committee for the David Geffen School of Medicine at UCLA since 2003.