

Partners *in* Discovery



Creating A New Environment To Rebuild Broken Brains

neu-ron

A brain cell that receives and transmits information and is responsible for the elemental brain functions that we observe, such as movement, language, sensation, and memory. Contrast this with glial cell, a brain support cell.

stem cell

A cell that can give rise to any cell type in the body and also to a cell just like itself. A stem cell is unrestricted in its potential to produce any other cell type.

pro-gen-i-tor

An immature cell that can give rise to many different types of cells. A progenitor cell is not a stem cell, because it is restricted; it can form only the cell types of one specific organ, such as the brain, liver, or skin.

CONT. PG 04

Istvan Mody, Ph.D. / Tony Coelho Professor of Neurology and Professor of Physiology
David Geffen School of Medicine at UCLA

Pregnancy, Post-partum Depression and the Brain

including postpartum depression (PPD), premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS). Let's see how this works.

GABA, a small amino acid synthesized in the brain, is the brain's major inhibitory neurotransmitter. When released from neurons, it binds to a variety of proteins called receptors. The activation of these receptors (GABAA) by GABA produces an inhibition of nerve cells by opening holes in their membranes that allow chloride ions to flow into the cells. GABAA receptors are the principal targets of several widely used synthetic drugs, including anesthetics; benzodiazepines (valium, for example); and alcohol. All of these substances

CERTAIN RECEPTORS LOCATED ON THE SURFACE OF NERVE CELLS IN THE BRAIN—specifically, those for the inhibitory neurotransmitter γ -aminobutyric acid (GABA)—change during the ovarian cycle and pregnancy. The changes are ovarian hormone-dependent and the malfunction of this process is thought to be the underlying cause of hormonally-linked mood disorders

Barbara Vickrey, M.D., M.P.H. / Professor and Vice Chair, Academic Affairs
Department of Neurology / David Geffen School of Medicine at UCLA

Better Outcomes:

Cutting-Edge Research
Extends To
Care Management

WHEN FACULTY IN THE DEPARTMENT OF NEUROLOGY make discoveries about better diagnostic tests and treatments for neurologic diseases, the job isn't done: those discoveries need to be made widely available to patients whose health they

will benefit—regardless of the patients' level of education, wealth, or primary language. New studies to dramatically re-engineer the traditional ways in which patients and families receive care for Alzheimer's disease, Parkinson's disease, and the prevention of stroke—and to test whether those re-engineered models of care improve patients' health—are underway, led by faculty in the department's Health Services Research Program.

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CONT. PG 07

Going the Distance



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

"If you want to go fast,
go alone. If you want
to go far, go together."

We are all well aware of the California State budget crisis and its impact on the University of California. Budget cuts for the university have been significant, as state funds have been reduced to help manage the shortfall in the state budget. The David Geffen School of Medicine at UCLA and our Department of Neurology have not been immune from the impact of these financial problems. This is not the first time that difficulties with state funding have taken a toll on the University of California and its five medical campuses. In the past, such budget issues have been short in duration and we are hopeful that will be true of the current crisis as well.

While what you may have read in the newspapers or heard on the news about the magnitude of the cuts to the University of California, I am pleased to inform you that the situation in the Department of Neurology at UCLA is nowhere near as severe as one might expect. There are a number of reasons for this fortunate situation. The UCLA Neurology Department receives only a small fraction of its total budget from state funds. The majority of the support for the department's activities comes from federal research grants and contracts, patient revenue, and philanthropy. None of these sources of income have been or will be affected by the situation in which we currently find the State of California. In addition, the federal stimulus funding extends directly to the National Institutes of Health. Last spring, NIH released a series of programs and requests for proposals to distribute stimulus funds for medical

research. The department responded rapidly and successfully, submitting 88 new research proposals directed at providing new insights and better treatments for patients with neurological disorders. Faculty members are already seeing success with these proposals, bringing new dollars to the quest to understand and better manage disorders of the nervous system. I am also happy to report that, while there was a transient reduction in philanthropic funds to the department associated with the downturn in the national and international economy, philanthropic gifts are now back to the level at which they were one year ago.

The message here is simple. The faculty, staff, and trainees of the UCLA Department of Neurology are steadfast in their determination to understand and treat patients with neurological disorders. The need to solve these problems, which affect millions of people worldwide, has never been greater. The California State budget crisis, the economic downturn of the nation, and the clamor over healthcare reform are all significant issues; but they have not had a significant negative impact—individually or collectively—on our ability to fulfill these important missions.

The following African proverb applies, "If you want to go fast, go alone. If you want to go far, go together." Our mission to succeed, with your partnership and help, remains unaffected. Together we will go the distance.

Art of the Brain Celebrates 10th Anniversary

Art of the Brain (AOB), a patient-driven non-profit organization that raises money for brain cancer research through the UCLA Neuro-Oncology Program, celebrated its 10th anniversary with a gala, The Art of Accentuating the Positive, at UCLA's Schoenberg Hall on Saturday evening, October 3, 2009.

Thanks in large part to the efforts of co-founder and brain cancer survivor Judi Kaufman, AOB has raised more than \$4 million for brain cancer research since its inception in 2000. The funds have enabled AOB co-founder and Board of Directors president Dr. Timothy Cloughesy to develop one of the premier brain cancer research laboratories in the world.

Two awards were presented at the event. On behalf of her family, Patty Balch accepted the Judi Kaufman Founder's Responsibility Award in honor of their son, Adam Balch, who succumbed to glioblastoma after a valiant 2 ½ -year battle. Dr. Albert Lai, Assistant Professor-in-Residence, Department of Neurology, received the Johnny Mercer Foundation Research Award for his commitment to translating his vital glioblastoma research into more effective therapies.

In addition to raising money for brain cancer, Art of the Brain raises public awareness of this deadly disease and spotlights the talent, strength, and courage of UCLA's brain cancer patients. ■



Above: AOB co-founder Judi Kaufman, flanked by Dr. Timothy Cloughesy (right); her husband, Roy (left); and Dr. John Mazziotta, Neurology Department Chair (far left)

Right: Judi Kaufman with the Balch family, recipients of the Judi Kaufman Founder's Responsibility Award





"Our only hope is to support leadership in science, with our hearts and imagination as well as our dollars."

A Rock Star of Science

Dr. Jeffrey L. Cummings Featured in "Rock Stars of Science" Campaign

Some of the nation's top scientific minds, including Dr. Francis Collins, Director of the National Institutes of Health, Dr. Rudy Tanzi, Professor of Neurology at Harvard University, and Dr. Jeffrey Cummings of UCLA joined with Aerosmith's Joe Perry, as the "Rock Stars of Science" (Rock S.O.S) campaign came to Capitol Hill for an unprecedented event at the Capitol Visitors Center Auditorium on September 24.

Rock S.O.S. is an ongoing philanthropic campaign presented by **Geoffrey Beene Gives Back®** to create awareness of and to address under-funding of medical research across diseases by highlighting the underlying "rock star" genius that drives scientific innovation.

The Rock Stars of Science who were honored included those leading the fight against Alzheimer's disease, the first mappers of the human genome, architects of treatment breakthroughs that made HIV a manageable condition, and researchers leading global fights against pandemics such as cancer.

In the GQ centerpiece that featured the Rock S.O.S., Dr. Jeffrey L. Cummings, M.D., Director of the Mary S. Easton Center for Alzheimer's Disease Research at UCLA Dr. Cummings, the developer of the neuropsychiatric inventory on brain function, is featured playing the acoustical guitar with singer Josh Groban and Dale Schenk, Ph.D., Executive Vice President and Chief Scientific Officer of Elan Corporation.

"This is our moment in history. An aging boomer generation that grows older and at greater risk for serious illness every year; historic levels of chronic disease; and the global spread of pandemics," explained Tom Hutton, Trustee of the Geoffrey Beene Foundation and CEO of Geoffrey Beene, LLC. "Our only hope is to support leadership in science, with our hearts and imagination as well as our dollars."

The Rock S.O.S. campaign was also featured in Vanity Fair, the New Yorker, Vogue and Condé Nast Travel. The Website www.rockstarsofscience.org features a declaration calling for more funding for science research which readers can sign and an option to nominate other rock stars. ■

Discovery and Hope Fiesta

UCLA's Mary S. Easton Center for Alzheimer's Disease Research held the first annual "Discovery and Hope Fiesta" on Sunday, September 13 at Avila's El Ranchito in Santa Ana. The event was hosted by Jay and Patti Glick, Jeffrey L.

Cummings, M.D., and Mario Mendez, M.D., to raise funds for Alzheimer's research and cognitive impairment.

The afternoon featured over 100 unusual silent auction items, including a concert cymbal signed by members of the rock band Incubus; a script from an "X-Files" episode signed by David Duchovny, along with agent Mulder's business card; a vintage 1993 Florida State leather jacket worn on an "Evening Shade" episode; and a football signed by NFL running back Eric Dickerson. The highlight of the afternoon was a live auction of two getaway weekends, a "Smart Car," and a cameo role in an upcoming episode of "Castle."

The "Smart Car" was purchased by Arthur Kassel, as part of a contribution from the Tichi Wilkerson Kassel Parkinson's Foundation, a foundation which honors his wife Tichi, who succumbed to Parkinson's disease.

Over 170 guests attended the event including many friends and business acquaintances of the Glick family. The event was the inspiration of Jay Glick in honor of his wife, Patti, who has been diagnosed with Alzheimer's disease. Jay is a founding partner of Montgomery Glick and Company, an accounting firm in Woodland Hills. The "Discovery and Hope Fiesta" raised net proceeds of \$50,000. ■

New Discoveries in Alzheimer's Disease

Scientific discoveries in Alzheimer's disease (AD) continue at a remarkable pace. New observations support the concept that accumulation of amyloid protein in the brain is the principal cause of AD. Two new risk genes that

increase the chance of getting AD both involve amyloid-related functions in the brain. New brain scans, called amyloid imaging, are able to reveal amyloid in the brain in normal elderly who are in the very earliest stages of AD; persons with mild memory changes; and patients with AD type of dementia. These images will assist in accurate diagnosis of AD, presymptomatic detection of AD, and monitoring treatment. These scans may eventually help us to prevent AD by identifying persons at risk for memory loss and allowing us to treat them before the disease progresses. Faculty members of the Mary S. Easton Center for AD Research are contributing to the great progress being made in understanding and treating AD. Dr. Liana Apostolova has developed new techniques for analyzing brain scans that allow us to predict which patients with mild memory loss will progress to AD type of dementia. Dr. John Ringman's studies of familial AD have demonstrated the effects of having the AD-causing mutation on brain function even before symptoms occur. Dr. Po Lu reported in a recent high profile publication that patients with mild memory impairment and depression respond better to treatment with donepezil than those with mild memory impairment and no mood changes.

The clinical trial program led by Dr. Josh Grill, supported by the Sidell-Kagan Foundation, has an exciting array of new drugs being tested for their ability to slow the progression of AD. Those interested in these advanced treatments should call UCLA's Easton Alzheimer's Center (310) 794-6039. ■

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STEM
CELLS

+

STROKE
RECOVERY:

Creating A New Environment To Rebuild Broken Brains

The Department of Neurology at the David Geffen School of Medicine at UCLA is taking a leadership role in stem cell and other mechanisms of brain repair treatments, which are promising avenues for the future in terms of ways to rebuild broken brains, says Jeffrey Saver, M.D., Medical Director, UCLA Acute Stroke Unit.

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As trials of molecules that improve the growth environment after stroke are about to enter the clinical realm, “the challenge is to provide a framework in which the right mix of chemicals and cells can encourage recovery networks,” he explains.

According to Saver, a revolution in the basic science of neurology over the last 15 years has led to tremendous advances in neuroplasticity and neurorepair. “We now know that the brain can be reshaped in adults.”

UCLA Clinical Trials Test Basic Science

New research programs are applying basic science discoveries toward human therapies. New discoveries in stem cell biology and the growth factor and chemical control of brain function are being tested in major new studies or in newly initiated clinical trials at UCLA. UCLA, in partnership with Stanford, has just been awarded a \$20-million grant from the California Institute for Regenerative Medicine (CIRM) to develop an FDA-approved stem cell therapy within the next four years for ischemic stroke (see sidebar). This is the largest State of California grant for stem cell research in stroke recovery. The University is one of five institutions in the country doing this type of research.

Three clinical trials are in the development phase and will begin trials at UCLA within the coming months. The first is a placebo-controlled study of a membrane precursor molecule, GSK 1172, which stimulates the sprouting of axons, or new neural connections. This must be administered within 72 hours of stroke onset.

The second trial involves Citicoline, a membrane precursor molecule that is a form of the essential nutrient, choline. Choline is an FDA-approved food supplement, but may have benefits in stabilizing the brain after stroke.

Within 24 hours of stroke onset, patients will get a daily dose of the drug for either six or 12 weeks to determine the most effective dosage.

A third trial will test the effect of one kind of stem cell, an adult stem cell, in its effect on recovery after stroke. This trial is still in the planning phases and will start in one year. It probably will be the first of several clinical trials for stem cell therapy in stroke.

Neural Repair Requires Clinical and Rehabilitation Treatment

The Acute Stroke Program at UCLA is a collaborative effort between Stroke Neurology and Rehabilitation Neurology. It represents the marriage of basic science and clinical trials.

Concurrent clinical, physical, and occupational therapy is necessary for neural repair, says Saver. Clinicians begin working with patients in rehabilitation two days after the onset of stroke, when the brain is critically ripe for cell restructuring.

“The brain can recover. It makes new connections; it is constantly changing, generating new pathways and connections. The patient is not just building muscles, but also channeling energy, making nerve cells functional,” he explains.

An important aspect of stroke recovery is repetitive activity, and Bruce H. Dobkin, M.D., Director, Neurological Rehabilitation Program at UCLA, has proven that the intensity of training is crucial to recovery: the more you do it, the more the brain learns. Just as in playing tennis or playing the piano, practice makes perfect.

Rehabilitation Neurology at UCLA is led by neurologists, rather than physiatrists. Saver believes that rehabilitation neurologists bring to the table greater knowledge of brain architecture, neurochemistry, and basic science. “The science behind the rehab has changed greatly over the last 15 years; there are more medications, and we have more tools.”

UCLA physician-scientists are hoping that advances in stem cell technology will add to the rehabilitation arsenal.



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Stem Cells 1.0

"There's a lot of hype about stem cells and brain repair," says S. Thomas Carmichael, M.D., Ph.D., co-principal investigator of the CIRM grant to use stem-cell technology for stroke therapy. "We do know that there is a period of time after a stroke in which the brain is plastic and can be treated for an improved recovery."

It has been shown that most primitive stem cells can morph into any type of cell (e.g. muscle, heart, bone, brain, etc.). In scientific models, injected stem cells will migrate to the injured area in stroke or other nervous system injuries. In the brain, these cells become neural progenitors, the next generation after the stem cells.

There are three ways to get stem cells into the brain: 1.) Neurosurgery, which delivers them directly to the region; 2.) spinal or brain fluid delivery, in which they are infused into the spinal fluid via a spinal tap or a brain catheter; and 3.) intravenous injection into the blood stream.

Carmichael explains that many progenitor cells move to areas of injury in the brain, no matter how they are introduced. "Unfortunately, most of these cells do not survive. When given intravenously, they tend to get stuck in the liver, spleen, or lung, and most die when injected directly into the brain. The cells that do survive often just sit there in a primitive state. They produce growth factors, but we need them to grow neurons or new connections."

In the planned clinical trials, UCLA is using current technology to test the effects of intravenous delivery. "These approaches have produced benefit in scientific models," says Carmichael, "but this early translational stem cell research will net a ceiling of modest benefit."

Stem Cells 2.0

How can stem cell therapies be improved to promote a more complete recovery? One approach is to engineer the stem cell environment to promote the survival and function of the cells. The CIRM grant represents a new approach to helping the cells survive, according to Carmichael. "We have to change the brain environment in order for stem cells to survive and to work." The grant will enable researchers to work with bioengineers to come up with new tissue engineering solutions to enhance survival and engraftment of the cells.

UCLA will also work with biotech companies to come up with a hydrogel patch or matrix. "Under traditional approaches, stem cells are shocked upon injection into the body. We want to use a synthetic matrix, or hydrogel, to help them survive the stress," he says.

"We also are working on cognitive enhancers—drugs that will enhance cognition and memory—and are testing them in scientific models. In addition to their benefit on stroke recovery alone, these cognitive enhancer molecules will likely support stem cell integration in the brain. We want to see if we can use the same mechanism to enhance stem-cell integration. This innovative use of biotech and pharmaceutical therapies is Stem Cells 2.0—the next wave in stem cell technologies."

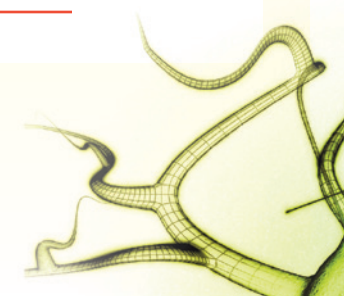
UCLA is uniquely positioned to make this happen. The University offers excellent clinical stroke care; research-based and clinical rehabilitation; and physician-scientists who span the entire spectrum and see opportunities at each tier. It is this novel collaboration that makes the Department of Neurology a particularly exciting place for the next generation of therapies. ■


UCLA Neurologist Part of Team Awarded \$20-Million State Grant to Use Stem-Cell Technology for Stroke Therapy

UCLA neurologist S. Thomas Carmichael, M.D., Ph.D., and Gary Steinberg, M.D., Ph.D., professor and chair of neurosurgery at Stanford University School of Medicine, have been awarded a \$20-million grant from the California Institute for Regenerative Medicine (CIRM) to develop an FDA-approved stem cell therapy within the next four years for ischemic stroke.

According to Carmichael, who is co-principal investigator, it is the first such effort to develop embryonic stem cells into a clinical therapy in stroke and the largest award in its category from CIRM. "This funding will position this effort as a leader in the field of translating stem cell technologies into human therapies for neurological disease by allowing us to address critical issues in the development of a human stem cell therapy for the brain," he said. "Basic science studies of stem cell therapies can show benefit in a neurological disease such as stroke, but lack the money, focus, and time to determine a definitive mechanism of action for these therapies in the brain, prove that they are safe for human use, and develop the strict manufacturing principles necessary for a clinical therapy." The team will investigate ways to use neural stem cells derived from human embryonic stem cells to ameliorate motor deficits that may arise when parts of the brain are deprived of oxygen when a blood vessel becomes blocked by a clot or an artery narrows, perhaps extending the window for effective treatment of the condition from hours to weeks or months after the incident.

The grant is part of a total of \$250 million awarded by CIRM's 29-member governing board to 14 multidisciplinary teams in California, Canada, and the United Kingdom. CIRM's Disease Team research awards are designed to quickly bring promising therapies to patients through teams that include basic scientists, clinicians, and industry. CIRM President Alan Trounson, Ph.D., said in a statement that the pace of the Disease Team projects stands in contrast to the decade or more that is usually required to reach clinical trials. "Scientists have talked for years about the need to find ways to speed the pace of discovery," he said. "By encouraging applicants to form teams composed of the best researchers from around the world, we think CIRM will set a new standard for how translational research should be funded." ■





The Power of
Philanthropy

Tom & Madeleine Sherak: It Feels Good to Give

"We've been especially pleased to have a home at UCLA."

The Sherak family: (left to right) Dan Glasser, Melissa Sherak Glasser, and Gabriella Resnick; Tom and Madeleine Sherak; Barbara and Paul Neinstein; Ginger and William Sherak. Grandchildren not pictured are: Jackson and Lilianna Glasser and Maya Resnick; Adam, Geordan, Jeremy, and Molly Neinstein; and Eloise Sherak.

Veteran fundraiser and motion picture industry executive Tom Sherak has specific thoughts about philanthropy. "I believe that people are basically good. Philanthropy is about convincing them that it will make them feel good to give," says Sherak, who consults for Marvel Studios and was recently elected president of the Academy of Motion Picture Arts and Sciences.

"It's not just that people are good," interjects his wife, Madeleine Sherak, who holds a Ph.D. in education and spent a decade teaching math in the Las Virgenes Unified School District. "It's that they want to be philanthropic, but many of them don't know how. Tommy helps direct that inner desire to be part of the philanthropic community."

The Sheraks know a thing or two about being philanthropic. After their daughter, Melissa, 37, a mother of four and UCLA alum with a Master's degree in Public Health, was diagnosed with multiple sclerosis at 15, the couple mobilized to help find a cure. They became active with the Southern California Chapter of the Multiple Sclerosis Society.

"People need to be presented with exactly what it is you're asking for. They want to give to something for which there is a personal connection," says Sherak, who, for 17 years as host of the chapter's annual Dinner of Champions, has rallied the entertainment industry to help find a cure for MS.

At the chapter's most recent dinner, Sherak, a former partner in Revolution Studios and chairman of 20th Century Fox Domestic Film Group, gave an impassioned speech that summed up the progress toward a cure, and what has happened thanks to time, talent, dedication, and funding: "Over the past 17 years, we have witnessed not only the most groundbreaking advances in the treatment of MS, but also the most comprehensive advances in helping people who are living with this disease. We have seen the

development of six FDA-approved, disease-modifying drugs used to treat MS, and the most cutting-edge research on the effects of Estriol on MS patients. We were there for the opening of the Marilyn Hilton MS Achievement Center at UCLA, and we have watched the incredible relationships develop between the doctors and researchers, and they have become our friends. Together, we have raised awareness, we have raised hope, and we have raised more than \$40 million."

Seventeen years ago, when the Sheraks wanted to extend their philanthropy beyond the MS Society in hopes of accelerating the search for a cure, they met with a development team at UCLA and asked, "Okay, what can we do?" UCLA suggested that they start a foundation for MS at UCLA, "Only we couldn't personally fund it," Sherak explains. "Although it was not the way UCLA usually did things—not the 'usual' foundation, in the University's terms—they were willing to try it our way. We would seed the foundation and see what would happen, if it would grow, and it has become a model. The money started to build and build. Grants have doubled and tripled the amount over the years. The foundation has become a good balance between the research and program and service sides—UCLA and the MS Society."

Tom Sherak believes the foundation's most significant accomplishment has been to provide the funds to hire Dr. Rhonda Voskuhl as Research Director of the UCLA Multiple Sclerosis Program. "The department chair at the time came to us and said he was trying to hire a researcher whom he

couldn't afford. He asked if he could use the money in our foundation to bring her to UCLA and we agreed. That was the greatest thing we ever did."

"I only wish we could help more people," says Madeleine. Our frustration is that so many people can't access the care logistically. People thrive at UCLA. To be able to connect the people and programs at UCLA to the people who need them, to be able to improve people's lives that way..."

"We've been especially pleased to have a home at UCLA," the couple concurs. "You know that everyone you come in contact with—every researcher, every doctor—is part of a team that's trying to figure it out."

Thanks to dedicated philanthropists like the Sheraks, UCLA's teams of physician/scientists continue to make progress toward finding cures for MS and other neurological diseases. ■

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, Director of Development, UCLA Department of Neurology, (310) 267-1837 or proderick@support.ucla.edu.

Better Outcomes: Cutting-Edge Research Extends to Care Management

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"We know that many people who have chronic diseases simply do not receive care that reflects our knowledge of research discoveries that will improve their health," says Dr. Barbara Vickrey, program director. One reason for this is the lack of time during physician visits to coach patients and empower them to become partners in managing their disease. Other reasons include lack of ways for doctors to regularly

follow-up with patients between visits to make sure they continue to take their medications, and very limited channels of communication between doctors and community agencies whose mission is to provide valuable services and education to patients and their families.

"To figure out how to design better systems for delivering care, our research starts with interviews of patients and families, to ensure we understand the barriers from their perspective. One of the striking findings is that while patients and families from poorer communities report more barriers than those from wealthier communities, what patients and family members from all backgrounds have in common are considerable unmet needs for information about managing their disease and substantial worry about the future," says Dr. Vickrey. It appears that for many neurologic conditions concerns about progression of the disease and about healthcare needs are common across social and economic strata.

Once the program's researchers have analyzed these barriers, "best practice" care protocols are designed by a team of neurologists, primary care physicians, nurses, social workers, and representatives from advocacy and service organizations for that disease and from the community in which these patients live. For example, the program's Dr. Karen Connor currently leads a VA-funded

"To figure out how to design better systems for delivering care, our research starts with interviews of patients and families, to ensure we understand the barriers from their perspective."

study to build a care management model for veterans with Parkinson's disease; she has engaged a team of neurologists from VA hospitals in the region and leadership from local Parkinson's disease, caregiver, and veterans' organizations. The re-engineered "care management" models all include nurses or social workers as care coordinators, who help physicians and patients stay on track with "best practice" protocols. "We tailor currently available electronic technology to produce reminders for care coordinators to proactively track and follow-up with patients, and we promote communication between patients, care coordinators, physicians, and community partners about new scientific discoveries. The goal is to make sure that no patient's healthcare issue 'slips through the cracks,'" says Dr. Eric Cheng, program faculty member.

Program research also focuses on patients in poor, underserved minority communities, for whom barriers to obtaining high quality neurologic care are magnified due to language, low education, and—in some cases—greater stigma associated with these conditions.

Researchers are building a "best practice" coordinated care model for preventing future strokes in stroke survivors in the Los Angeles County public safety net system; the goals are to control risk factors such as high blood pressure and elevated cholesterol, and to obtain proof as to whether the new way of delivering care reduces the risk of stroke. According to Dr. Vickrey, it will not be enough to prove that the new model lowers the risk of future strokes and heart attacks: the research also includes a cost analysis, so that policy makers have the information they need to make decisions about sustaining a successful stroke prevention care model. "Our ultimate goal is to widely export successful, sustainable models that we have proven result in better patient outcomes." ■

Barbara Giesser, M.D. / Professor and Vice Chair, Education & Clinical Affairs
Department of Neurology / David Geffen School of Medicine at UCLA

Why I Do This

I'VE ALWAYS WANTED TO BE A DOCTOR, for as long as I can remember. The brain is one of the last great frontiers of medicine, which is why I got into Neurology. I became a specialist in multiple sclerosis, a degenerative disorder of the brain and spinal cord, by accident. When I finished my residency, I was offered a position at a big MS care center headed by a very famous MS specialist, Dr. Labe Scheinberg. He was a neurologist and educator who helped pioneer new ways of treating people multiple sclerosis. His center became a prototype for similar centers across the country. I couldn't have picked a better place to train. Dr. Scheinberg's philosophy was to treat the whole patient. He was among the earliest advocates for bringing neurologists, psychologists, rehabilitation specialists, and other health care professionals together to address the problems of patients with MS in a comprehensive way.

During the past 20 years, there have been extraordinary advances in the diagnosis and treatment of MS. Every time I see a patient, there is usually something I can do to help them. I can change their medication to alleviate a symptom; I can prescribe agents to help limit nerve damage; I can explain the disease or its symptoms to a family member to make it less frightening; I can access the resources of the UCLA Marilyn Hilton MS Achievement Center. Primarily, I can empower patients to take charge of their health.

People don't realize it, but the word "doctor" comes from a Latin word that means "teacher." That's what we do; we give information, tools, and strategies that help give patients a measure of control over an unpredictable neurological disorder.

Most neurologists deal with chronic things that are incurable but treatable. I view the course of treatment as a journey—a road the patient and I will walk down together. I give patients tools to help them take charge of their disease. That's the essence of what I do. There is always hope, always something to do. I key into that potential for hope. That's why I do this. ■



"The brain is one of the last great frontiers of medicine, which is why I got into Neurology."



Chelsea's Hope: Grass Roots Effort for a Cure

Lafora disease, also called Lafora progressive myoclonic epilepsy, is a rare, progressive and degenerative form of epilepsy that strikes children between the ages of nine and 14.

Inherited through recessive genes, Lafora causes seizures, muscle spasms, difficulty in walking, dementia, and is eventually fatal. Most therapy is primarily aimed at reducing seizures. Although seizures can be controlled for a long period of time by the use of antiepileptic drugs, patients rarely survive beyond 10 or 20 years due to the devastating effects of dementia and ataxia. Because Lafora is considered to be an "orphan" disease, it gets little federal funding; yet researchers are at a pivotal point in their understanding and treatment of the disease. A nonprofit organization called Chelsea's Hope, created with the help of a friend by a family whose child was diagnosed with Lafora, is helping to raise the funds necessary to facilitate research and find a cure.

Chelsea Gerber is a beautiful young woman of 19, who was diagnosed with Lafora disease when she was 14 years old. A family friend, Barb Goldsmith, wanted to do something for Linda and Howard Gerber and their daughter. Barb

met with researchers at UCLA about starting a foundation and raising funds. When she learned there were people all over the world trying to cope with Lafora, she created a Web site designed to educate others about this devastating disease, share information, and offer support. Almost two years ago, Chelsea's Hope was officially launched, and other families quickly became involved.

Considered a "lifeline" for families whose children have been struck by this rare adolescent disease, Chelsea's Hope held its first public fundraiser on May 17, 2009 at Forli Restaurant in Alamo, California for a standing-room-only crowd of 130 guests. Dr. Antonio Delgado-Escueta and Dr. Eain Cornford, professors of Neurology at the David Geffen School of Medicine at UCLA and renowned experts on Lafora, attended the event and presented a video on the disease, its effects on the brain, and current research being done. The event generated proceeds of nearly \$30,000.

"It is through contributions such as these that my colleagues and I can step up the pace to

more fully understand this devastating condition and thus bring innovative care to those who suffer from it," said Delgado-Escueta.

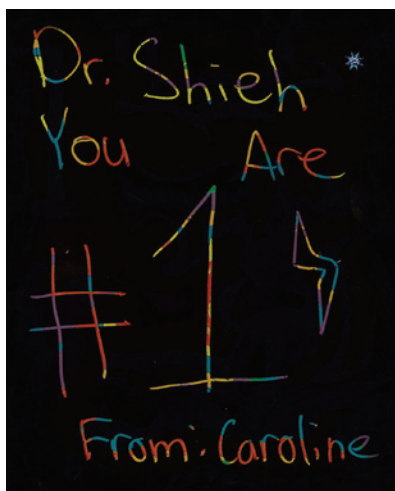
In the 18 months since the inception of Chelsea's Hope, more than \$163,000 has been raised for UCLA research. According to Dr. John C. Mazziotta, Chair, Department of Neurology, David Geffen School of Medicine at UCLA; Director, Brain Mapping Center; and Associate Director, Semel Institute for Neuroscience, unrestricted funds such as those provided by Chelsea's Hope are vital to the success of research in the modern era. They enable researchers to take a "sound hypothesis and a modest amount of data and make a scientific leap." Such leaps advance the field, he says, "and provide breakthroughs that typically are not realized by the more traditional mechanisms." He calls it "innovative funding for innovative research." ■

For more information on Chelsea's Hope, visit www.chelseashope.org.



Perry Shieh, M.D., Ph.D.

Assistant Clinical Professor of Neurology
David Geffen School of Medicine at UCLA



Neuromuscular Disease:

Improving Quality of Life While Finding a Cure

EVERYONE COMING TO THE UCLA Neuromuscular Clinic asks me two questions: 1) what do I have? and 2) what can we do about it? As research progresses in the field of Neuromuscular Disease, our answers to these questions become better and progressively more optimistic. The goal of our clinics is to improve, or at least preserve, the quality of life for our patients as we try to find cures for their diseases.

The research in the field of peripheral nerve and muscle disease has exploded in the past 10 years. New neuromuscular diseases are being named every year as we develop a better understanding of the causes associated with these diseases. Active research in many forms of muscular dystrophy, neuropathy, Lou Gehrig's Disease (also known as ALS), and myasthenia gravis has not only resulted in a better understanding of their causes, but also brings us closer to better treatments, ranging from gene therapy and drug development to stem cell strategies.

Perhaps the best example of evolving treatments is in the field of muscular dystrophy. Duchenne Muscular Dystrophy (DMD), for instance, is a muscle condition that affects boys, causing progressive muscle weakness. This condition is the result of malfunction of a gene known as Dystrophin. Normal muscle should have an abundant amount of the Dystrophin protein, but muscle biopsies of boys with DMD show no Dystrophin protein. There are many ways that the Dystrophin gene may have been damaged. Recent strategies have focused on patching the gene so that some Dystrophin protein can be made in patients with DMD. They have already shown that some of these techniques work in a scientific model and the next step will be to figure out how to use these strategies in humans. UCLA is actively participating in international efforts to test these techniques and, in the near future, to provide successful therapies to patients with DMD.

There are many other promising treatments for other diseases, including other muscular dystrophies; ALS; certain forms of neuropathy; and myasthenia gravis.

There is much active research in the field of neuromuscular diseases at UCLA and at other institutions, and UCLA collaborates in international efforts to identify good treatments through clinical trials.

As our treatments improve, hope for all of our patients also improves. While new and emerging medical treatments provide great promise for our patients, our clinics are there to support them. Our multidisciplinary team of physicians and allied health professionals are working towards preserving function, mobility, and quality of life. The ALS clinic, for example, maintains a staff of neurologists, a physical therapist, an occupational therapist, a speech therapist, and a respiratory therapist. The staff of our new multidisciplinary muscular dystrophy clinic includes a neurologist, a pulmonologist, a cardiologist, an orthopedic surgeon, an orthotist, and a respiratory therapist. Their efforts are not only good for the patient, but also serve as an optimal bridge to new emerging treatments. ■

Pregnancy, Postpartum Depression and the Brain

CONTINUED
from COVER →

enhance the effect of GABA at its receptors, thus increasing the inhibition of nerve cells. No wonder anesthetics are being used to put people to sleep, and valium to make them drowsy. Yet, the brain itself can synthesize

chemicals capable of enhancing inhibition through GABAA receptors. These compounds, called neurosteroids, can act as the brain's own anesthetics. They are produced in the brain from steroid hormone precursors (glucocorticoids, the stress hormones; or progesterone, the hormone produced by the ovaries). It follows that whenever the levels of stress hormones or ovarian hormones change in the body, the levels of neurosteroids in the brain follow suit. The biggest changes in ovarian hormones take place during pregnancy. Progesterone levels become elevated by over 100-fold compared to normal. The levels of neurosteroids (produced in the brain from progesterone) that enhance inhibition are increased accordingly. Very high levels of neurosteroids in the brain are dangerous. Just like anesthetics, they might enhance inhibition to such an extent that most pregnant mammals would be sedated during much of their pregnancy. To avoid this, the number of GABAA receptors sensitive to the progesterone-derived neurosteroids decreases, so that the high levels of neurosteroids are balanced out by fewer GABAA receptors.

We have carried out experiments in a scientific model that show exactly this pattern of hormone/GABA receptor balance. However, this balance in the mother's brain tips over just after delivery. At this point, progesterone levels drop precipitously, as do the levels of brain neurosteroids. This sudden change catches the reduced number of GABAA receptors off-guard. Without the neurosteroid enhancers, the few GABAA receptors that were necessary to prevent sedation during pregnancy cannot fulfill their inhibitory role during the postpartum stage. The result is a period of increased neuronal excitability until the number of GABAA receptors is restored to pre-pregnancy levels.

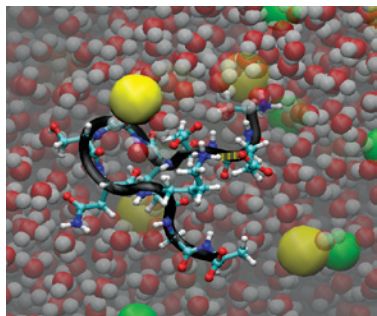
In our experiments, we found that if the process of recovery of GABAA receptors is delayed, depression-like behavior ensues. This behavior is ameliorated by the use of a drug that specifically enhances the function of the GABAA receptors that did not have a chance to be restored to normal levels.

By developing the first model of PPD, we have gained considerable insights into the fundamental mechanism of this debilitating neuropsychiatric disorder that, according to some estimates, affects more than 10% of women after giving birth. Using the model, we aim to develop novel and specific therapies for PPD, and possibly for PMDD, a form of irritability and anxiety that is also linked to periods of changes in progesterone levels over the menstrual cycle. Our hypothesis is that the regulation of neurosteroid-sensitive GABAA receptors on the surface of nerve cells is the culprit in both disorders. Our goal is to refine the research at the bench, to apply it in a clinical setting, and ultimately to cure the cause, not just the symptoms of these debilitating disorders. ■

MEET A SCIENTIST

David B. Teplow, Ph.D.

It takes more than a village to find a cure for neurological diseases and disorders. It's an arduous journey from bench to bedside, and UCLA's Neurology labs are filled with many talented and dedicated scientists you never see. That's why, over the coming months, we'd like to introduce you to some of them in this column.



Dave Teplow, Professor of Neurology at the David Geffen School of Medicine at UCLA and the head of our Biopolymer Laboratory, is working on a vital step in finding a cure for Alzheimer's disease. We think he is the antithesis of the stereotypical science nerd. Here is a basic scientist who manages not only to explain the very technical things he does in terms an ordinary person can understand, but also to make the subject fun. His enthusiasm is infectious. Passionate about his chosen career and grateful for the private support that makes it possible, Dr. Teplow claims he's "never had a real job." How cool is that?

First of all, what is a Biopolymer Lab and what do you do there?

Our lab seeks to understand how the Amyloid Beta (A β) protein causes Alzheimer's disease. We know that A β sticks to itself to form structures ("aggregates") that kill nerve cells, but we don't know the exact shapes of these aggregates. We need to know their shapes in order to design new classifications of drugs to cure Alzheimer's. We do this in two ways:

We chemically synthesize A β in the lab and study how it forms the shapes that cause nerve cell death.

We use computers to create a virtual brain, and then we place A β in this brain and look at how all the atoms in A β move. We see that certain atoms are always close to each other. We want to prevent them from coming in contact.

We also use the computer to design drugs that fit between the atoms that form the A β structures. On the computer screen, A β initially looks like rope. However, this rope coils up and sticks to other coils, producing what are called "oligomers." It is these oligomers—particularly clusters of five to six of these coiled ropes—that are thought to cause Alzheimer's disease. That's why it's important to learn how the initial structures form.

How close are we to creating a drug that will cure Alzheimer's?

There are tons of drugs out there, but so far, none of them have been curative. There are no drugs that will reverse and prevent Alzheimer's. The work we are doing will allow us to develop a new classification of drugs that will block the progression of Alzheimer's and, hopefully, in the future, prevent its development in the first place.

How long will that take?

Science doesn't work quickly. However, this is the first time in over a hundred years since the disease was discovered, that the time scale for clinical trials can be measured in years as opposed to decades.

Wow. That's something. How many people are involved?

It takes a team to create a virtual brain. It's laborious, tedious work that involves physics and computer programming—doing simulations takes months or longer, even with super computers. It's a feat in itself to set them up, then you wait while the system recreates what goes on in the body. Effectively, the computer takes tens of millions of snapshots of A β in the brain, all of which must be analyzed. The complexity is like looking at a crowded dance floor onto which a strobe light is flashing on and off. All these bodies moving in a crowded space—what do they look like? Only instead of people, they are proteins.

We feel very lucky to be able to have the ability as well as public and private support to be able to do the work. Two research grants, among many, have been key to this process: a grant from the National Institutes of Health (NIH) for the "structural and kinetic analysis of A β fibrillogenesis;" and a grant from the James Easton Consortium for Alzheimer's Drug Discovery and Biomarkers at UCLA on "Targeting the cause of Alzheimer's disease: A combined computational and experimental strategy for the design of novel therapeutic compounds." We also participate in a program headed by Dr. Giulio M. Pasinetti, Mt. Sinai School of Medicine, and funded by the NIH Centers for Excellence in Research on Complementary and Alternative Medicine, on the protective roles of grape extracts in Alzheimer's disease. Red wine, often called aqua vitae (water of life), contains anti-oxidants that may be effective in the treatment of Alzheimer's disease.

How did you get into this field, and what brought you to UCLA?

I always wanted to do biomedical research. I was a biochemistry major and got a Ph.D. in cancer biology. My early post-doc work was in mad cow disease. I've studied brain function and disease for 30 years—but in the last 20 I focused on Alzheimer's. I came to UCLA five years ago from Harvard Medical School because of UCLA's superb combination of clinical neurology and basic science practice. ■

Chen Family Neurology Symposium Held



The Fu-Hsing and Jyu-Yuan Chen family is committed to neurological research and community education, which led to a major, multi-year gift from the family's foundation to the UCLA Department of Neurology for the study of Parkinson's disease and other related disorders. The third annual Chen Family Neurology Symposium, which was held on October 3, 2009 in the Neurology Research Building at UCLA, is an excellent example of the family's dedication to research and education.

More than 150 members of the Chinese-American community heard presentations on Alzheimer's disease, stroke, and Parkinson's disease. Each presentation was given by the program director: Jeffery Cummings M.D., Ph.D., spoke on Alzheimer's; Jeffery Saver M.D., Ph.D., talked about stroke; and Jeff Bronstein M.D., Ph.D., discussed Parkinson's disease and related disorders.

Mr. Frank Chen opened the symposium with brief remarks about continuing his family's philosophy of "giving back." Dr. Bronstein concluded with praise for the Chen family. "We remain grateful for the research advances that the Chen Family Foundation gift has allowed us to achieve, and we are grateful for the family's friendship." ■

Did You Know?

You can make tax-free gifts from your IRA!

The IRA Charitable Rollover created under the Pension Protection Act of 2006 has been extended through the end of 2009. Donors who are 70½ years of age or older may make a charitable gift from a traditional or Roth Individual Retirement Account (IRA) of up to \$100,000 per year tax free. To qualify for IRA Charitable Rollover, the donor must direct the IRA manager to transfer funds directly to The UCLA Foundation. The IRA Charitable Rollover option is set to expire on December 31, 2009.

For more information about ways to take advantage of this important giving opportunity, please call the UCLA Office of Planned and Major Gifts at 800.737.8252 or emailing giftplanning@support.ucla.edu, or visit www.giftplanning.ucla.edu. ■

Wish Upon a Star



We've told you about some of our programs, our faculty, and our donors—the things we're doing and the people who make it all happen. However, cutting-edge research requires sophisticated equipment. It's expensive, but not when you consider the results it may bring. Your generosity can provide the Department of Neurology with unrestricted funding to meet its most urgent needs. Following are a couple of our highest equipment priorities—our most pressing wishes—for your consideration. We hope you'll help us do more than "wish upon a star." Thank you.

Portable Comprehensive Sleep System

★★★★★

A donation of \$20,000 will pay for this comprehensive system that records Sleep Studies in pre-op patients and patients who are sick with neurological disorders. The system is designed to diagnose and manage Sleep-Related Disordered Breathing, including Obstructive Sleep Apnea, Central Sleep Apnea, and Nocturnal Hypoventilation Syndromes, all of which need CPAP/Bipap respiratory assistance equipment.

Confocal Microscope

★★★★★

The Neuroscience Discovery Program is in need of \$50,000 to purchase a confocal microscope that would enable our researchers to show changes in fluorescently labeled receptors on the surface of nerve cells. These specific receptors for the inhibitory neurotransmitter GABA change during the ovarian cycle and pregnancy. The changes are ovarian hormone-dependent and the malfunction of this process is thought to be the underlying cause of hormonally linked mood disorders including PMDD/PMS and postpartum depression.

If you are interested in more information to make these wishes come true, please contact **Patricia Roderick**, Director of Development, Department of Neurology, UCLA Medical Sciences Development. Direct line: (310) 267-1837 or proderick@support.ucla.edu. ■

In Memoriam.

The Department of Neurology is sad to belatedly report the passing of two very supportive donors.

Franklin Otis Booth, Jr., a former Los Angeles Times executive and businessman whose early investment in a venture headed by a young Warren Buffett laid the groundwork for his great success, died on June 15, 2008 at 84.

Mr. Booth, also known as "Otis," was a philanthropist and great-grandson of Gen. Harrison Gray Otis, founder of the Los Angeles Times. He died at his Los Angeles home of complications from ALS, also known as Lou Gehrig's disease. Survivors include his wife, Lynn; a son and a stepson; three daughters and a stepdaughter; and 15 grandchildren.

Mr. Booth oversaw the printing of the Times during the 1950s and was named corporate vice president of Times Mirror Corp. in 1968, responsible for forest products and commercial printing. After his retirement in 1972, he operated several businesses before turning to citrus farming and raising livestock. Booth Ranches in the San Joaquin Valley encompass 9,000 acres of orange groves, the two citrus packing houses of Otis Orchards, and a cattle ranch.

Mr. Booth's commitment to philanthropy both during his life and through the legacy he established with the Otis Booth Foundation has significantly benefited many institutions in the Los Angeles area, including the UCLA Department of Neurology, for which we are extremely grateful.

Jack Goldberg was laid to rest on July 27, 2008 at the age of 95. Born in Los Angeles on August 26, 1913, Mr. Goldberg was a real estate investor in the Los Angeles County area and an avid writer, whose short stories and poems were published.

Mr. Goldberg's true devotion was to his wife, Shirley, who predeceased him in 2007. Married for 48 years, the Goldbergs are buried at Mt. Sinai Memorial Park. Mr. Goldberg was very involved in charitable work, especially that dealing with Alzheimer's disease. The Shirley and Jack Goldberg Trust included a significant bequest for Alzheimer's research at UCLA under the direction of Dr. Jeffrey Cummings. ■

Department of Neurology

Attention: Roberta Rey
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Los Angeles, CA 90095

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Meet Our
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UCLA



Roongroj Bhidayasiri, M.D. F.R.C.P.

A NATIVE OF THAILAND, DR. BHIDAYASIRI DID HIS NEUROLOGY RESIDENCY AT UCLA, followed by a fellowship in Movement Disorders. He returned to his native Thailand in 2005 to establish the Chulalongkorn Comprehensive Movement Disorders Center, the first of its kind in the country. This alum is fascinated by the cello, which he plays as a hobby (Bach's Prelude is his favorite piece). A big picture of Yo-Yo Ma hangs in his office.

I went to Chulalongkorn University in Thailand, where I graduated in medicine in 1994. I then trained in Internal Medicine and Neurology at University of Oxford and London teaching hospitals until 1998, when I obtained my MRCP (UK), the equivalent of certification by the American Board of Internal Medicine.

I moved to the U.S. in 2000 to start my Neurology residency at UCLA, followed by a fellowship in Movement Disorders with Jeff Bronstein. I moved back to Thailand in 2005 to establish the first Movement Disorders center in Thailand: Chulalongkorn Comprehensive Movement Disorders Center. In 2008, I was nominated to be a Fellow of the Royal College of Physicians of London. The organization was founded in 1518 and was the first medical institution in England to receive a Royal Charter.

Currently, I am an associate professor of Neurology and a director of the Chulalongkorn Comprehensive Movement Disorders Center, which is the first center in Thailand specializing in Parkinson's disease and related disorders. I am a principal investigator of the Parkinson's disease registry in Thailand, an investigator of a number of phase 2-3 international clinical trials on new therapeutics for Parkinson's disease, and the most recent stem cell research on PD utilizing the IPS technology. I am the main author of the best-selling textbook, Neurological Differential Diagnosis, published in 2005 by Blackwell Oxford. I also co-edited the textbook, International Neurology, launched in October 2009 by Wiley-Blackwell and endorsed by the World Federation of Neurology (WFN).

I am proud to be a UCLA Neurology alumnus. I considered myself lucky to get into the UCLA Neurology residency program. Training at UCLA gave me further in-depth training on top of the basics I learned at Oxford and London. I love what I do: helping patients with abnormal movements—particularly PD—to get better; being involved in PD research; and teaching medical students, residents, and fellows.

I feel very indebted to Dr. Mazziotta, Jeff Bronstein, and other faculty members for the continual support and advice they have provided me with throughout my career. It was the model I learned at UCLA that enabled us to start the fellowship training program in Movement Disorders at Chulalongkorn. I visit Jeff Bronstein's lab every six months to keep myself updated. My plan is to establish research collaborations between UCLA and Chulalongkorn Comprehensive Movement Disorders Center.