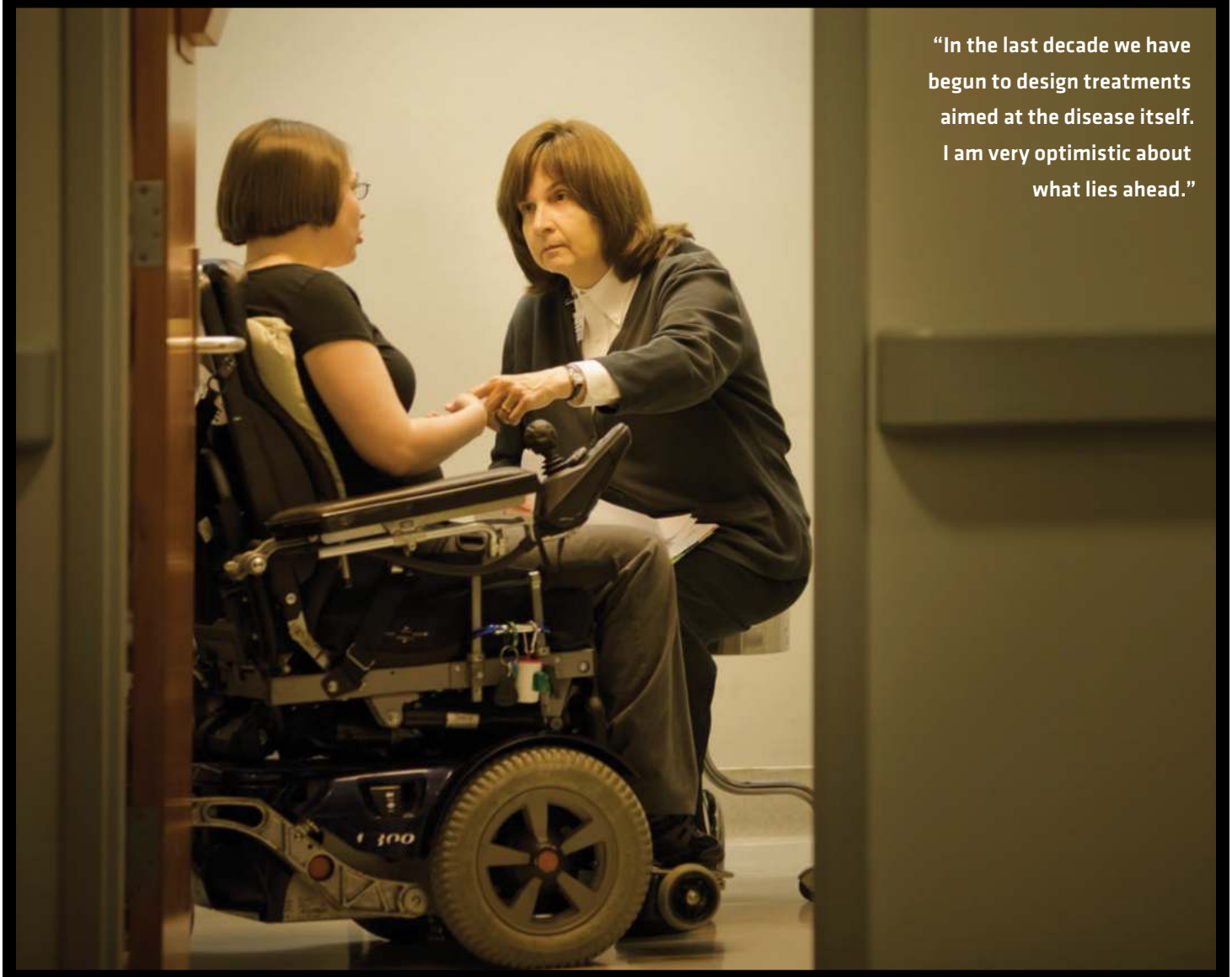
PARTNERS IN Discovery

UCLA NEUROLOGY NEWSLETTER × SPRING '09



"In the last decade we have begun to design treatments aimed at the disease itself. I am very optimistic about what lies ahead."

LETTER FROM THE CHAIR

PROSPERING AMID HARD TIMES

THESE DAYS IT'S HARD to read a newspaper or watch a news telecast without feeling depressed. The failing economy, two major wars, violence, unrest and economic instability dominate the headlines. Health care has not been immune from these difficult times. The number of uninsured individuals in the United States continues to climb and will grow further as unemployment increases. The National Institutes of Health (NIH) is facing challenging times, with reduced funding and the requirement to make difficult decisions about which areas to support.

But in the world of medical research, particularly research relevant to neurologic diseases, the news could not be better. For the last three decades, 30,000 basic neuroscientists have been studying normal brain function and how it is altered by disease. This monumental effort is now poised to deliver better and safer treatments and, ultimately, cures for disorders that, only a few years ago, seemed impenetrable. The process is accelerated by electronic communications and Web-based systems that allow instantaneous sharing of new scientific information about neurologic diseases on a worldwide basis. Another, less likely means of accelerating research and discovery in neurologic disease is that we now know that an insight into one disease may provide important clues for another. Thus, a new observation about protein accumulation in the brain cells of patients with Alzheimer's disease may inform individuals studying other disorders like Parkinson's, Huntington's or Lou Gehrig's diseases.

The future is very promising for the development of new treatments for patients with disorders of the nervous system – and UCLA can and will take a leadership role in this process. Our Department of Neurology is one of the three largest in the world, affording us the opportunity to care for patients and study diseases across the full gamut of neurological disorders. Our faculty are accomplished and have maintained their No. 1 ranking in NIH funding for the last six years. The size of the department also enables us to take observations from the clinic and bring them to the laboratory, where new treatments can be developed and then tested in patients in experimental clinical research trials.

When times are tough, the resourceful emerge with new ideas and new ways of doing things. *Partners in Discovery* was developed for just such times. The faculty, trainees and staff of the UCLA Department of Neurology are ready to deliver on the 30 years of effort that they and others have put into this process. With your philanthropic support, we will have the means to not only weather these difficult times, but to excel. Faculty who might not consider relocating to UCLA in normal times would be intrigued by such an offer when times are tough. Space and resources left vacant by disciplines outside neurology that are not as robust could be populated by successful faculty with important research ideas. It will be up to us, collectively, to make a difficult situation into a successful one. I am confident that we will succeed.

John Mazziotta, M.D., Ph.D.
Chair, Department of Neurology
Stark Professor of Neurology

NEUROLOGY IN THE NEWS

Could Red Wine Prevent Alzheimer's Disease?

David Teplow, Ph.D., professor of neurology, made exciting recent discoveries suggesting that compounds found in red wine known as polyphenols may offer protection against Alzheimer's disease. Dr. Jeffrey Cummings, professor of neurology and director of the Mary S. Easton Center for Alzheimer's Disease Research, discussed the research in a television news segment that aired on 22 CBS affiliates nationwide.

Understanding Children, Teens and Young Adults

Many of the intellectual and emotional changes that occur in children, teens and young adults can be explained by the recent findings of Paul Thompson, Ph.D., professor of neurology and member of the Laboratory of Neuro Imaging, into how a brain matures. Dr. Thompson's research was featured in a *New York Times* article. His important work is also reported in "The Teen Brain," published in the September issue of *Harvard Magazine*.

Can a "Sleep Watch" Determine the Best Time to Wake Up?

UCLA sleep expert Frisca Yan-Go, M.D., director of the UCLA Sleep Disorders Center in Santa Monica and professor of neurology, commented in a CBS-affiliate news segment on a sleep-tracking watch that makers claim can determine the optimal time to wake people from sleep.

Identifying Strokes to Save Lives

Bruce Ovbiagele, M.D., associate professor of neurology and director of the Olive View/UCLA Stroke Program, was quoted in an article on Alternet.org about identifying the warning signs of strokes. Read what he said and learn a simple formula for identifying strokes.

For links to the articles and broadcasts referenced above, go to www.neurology.ucla.edu/html/Department/Newsletter/PIDN_Spring09.html.

KUDOS

MARIE-FRANCOISE CHESSELET, M.D., Ph.D., professor of neurology and chair of the Department of Neurobiology, has been awarded a National Institute of Environmental Health Sciences five-year center grant. Dr. Chesselet, together with three Department of Neurology faculty (Drs. Jeff Bronstein, Ming Guo, and Beate Ritz) and other UCLA colleagues (Drs. David Krantz, Nigel Maidment and Michael Levine), will study how environmental factors contribute to the cause of Parkinson's disease. "Work in the center builds on the unique strengths of epidemiology and genetic studies at UCLA to develop treatments that improve not just the symptoms, but the progression of the disease," explains Dr. Chesselet.

MING GUO, M.D., Ph.D., associate professor of neurology and molecular and medical pharmacology, won the prestigious 2008 National Klingenstein Fellowship award. "I am very excited to receive the support from the Klingenstein fund and very encouraged to be chosen as the Robert H. Ebert Clinical Scholar," Dr. Guo says. "I hope that our work will provide significant understanding about the genetic basis of Alzheimer's and Parkinson's diseases, as well as epilepsy, and will help to lead to new treatments for patients with these devastating diseases."

BARBARA VICKREY, M.D., M.P.H., professor of neurology, received the Alzheimer's Association, California Southland Chapter's "Researcher of the Year" award. "Until there is a 'cure,' Alzheimer's disease patients and their caregivers need access to the medical care and community services that scientific studies have shown will maximize their health and quality of life," says Dr. Vickrey.

INTRODUCING...

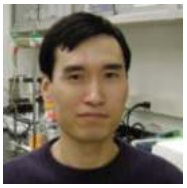
SHAMSHA A. VELANI, M.D.

Dr. Shamsha A. Velani feels right at home in her new position as assistant clinical professor in the UCLA Department of Neurology's Neuromuscular Division.

Dr. Velani is a general neurologist who sees patients grappling with neuromuscular problems, ranging from back, arm, or neck pain to weakness, spinal concerns, and inherited muscle and nerve disorders. These are often complex cases, many of which have been referred after the patients have seen multiple physicians. In addition to treating patients, Dr. Velani conducts electromyography (EMG) studies to help diagnose the source of patients' neuromuscular problems. She also continues to have an interest in epilepsy, particularly as it affects women – including issues of fertility and hormonal changes that accompany the disorder.

"My parents had their health care at UCLA even before I started here and I was so impressed with the quality of care they received that when the opportunity to become part of that team presented itself, I was very excited," Dr. Velani says. "UCLA has been a huge part of my life growing up and I feel honored to now be part of the system and to treat people at the place where I was once a student."

ZHEFENG GUO, PH.D.



As a graduate student at Peking University in Beijing, China, and then at UCLA, where he earned his Ph.D., Dr. Zhefeng Guo studied protein structure, using a technique known as electron paramagnetic resonance (EPR) spectroscopy to learn more about how proteins fold into the three-dimensional structures that enable them to perform their functions. In the course of these studies, Dr. Guo became interested in how the process goes awry. In cases of protein misfolding, proteins such as beta-amyloid can aggregate and form the plaques that are associated with Alzheimer's disease. Misfolding proteins are also believed to be a factor in other neurodegenerative diseases such as Parkinson's and Huntington's diseases.

Dr. Guo, who joined the Department of Neurology faculty as an assistant professor after completing his postdoctoral fellowship at UCLA, is now the principal investigator of a study in which he is developing a new approach to using EPR spectroscopy to examine the structure of beta-amyloid, the primary component of the plaques found in Alzheimer's disease patients. The new EPR approach could also be used to study other diseases, including Parkinson's and Huntington's diseases.

The desire to learn more about these diseases so that new strategies might be developed to prevent them is what drives Dr. Guo in his daily work. "It's very rewarding to make discoveries that contribute, even in small ways, to something that's really important," he says. "You leave a trail behind you and then a few years later you are able to look back and see that you did something important for science, and for humanity."

Glimmers of Hope

Dr. Susan Perlman has devoted her career to improving the lives of her ataxia and Huntington's disease patients. Finally, there is cause for optimism.

By Dan Gordon

PAUL KONANZ NEVER THOUGHT he would be hanging out at professional meetings for neurologists. But when his daughter Brianne was diagnosed with Friedreich's ataxia in 1986 at the age of 9, Konanz, an electrical engineer with an M.B.A., began to make it his business to learn as much as he could about the rare genetic disorder and the work being done by physicians and scientists in an effort to improve the lives of people such as Brianne.

Friedreich's ataxia is an inherited, neurodegenerative disorder characterized by progressive loss of balance, coordination, speech, muscle strength, and heart function. It is one of dozens of hereditary ataxias, and the most common to be diagnosed in childhood and adolescence.

Brianne began using an electric scooter in middle school and needed an electric-powered wheelchair starting in high school. By then her speech had begun to slur. Now 31, she has a caregiver who drives her, a service dog, and a ceiling track system that transports her around her house. "She has remained true to herself," asserts her father. "Brianne is a remarkable woman who lives life as abundantly as she can." That includes sky-diving and sit-down skiing. Brianne eats well and exercises regularly. "She wants to stay as healthy as possible so that when there is a treatment that can stop the progression, she will have as much quality of life as possible," Paul Konanz says.

For the last two decades, Konanz, whose family lives an hour north of San Francisco, has been in regular contact with Susan Perlman, M.D., professor of neurology at UCLA and Brianne's neurologist. Any time he attends a professional meeting, she is there. But Konanz never expected to see Dr. Perlman in the hotel lobby as late as he did one night at the annual meeting of the National Ataxia Foundation a few years ago.

"All of the presentations and networking events were over, and Dr. Perlman never struck me as a partier, so I asked her what she was doing down there so late," Konanz says. He pauses to collect himself. "When I think about what she said it always makes me well up. She said she wanted to make sure there wasn't a parent down there who had a question she could answer."

AFTER NEARLY 30 YEARS of studying and treating neurogenetic disorders, during which she has built the nation's largest clinical practice for patients with various ataxias, as well as one of the largest for patients with Huntington's disease, Dr. Perlman is optimistic that she and her colleagues are finally beginning to see the fruits of their labor – and hopeful that the Konanzes and other families she has gotten to know so well over the years will be able to benefit.

Dr. Perlman, director of the UCLA Clinical Neurogenetics Program (which includes both the Ataxia Center and the Huntington's Disease Center of Excellence), began studying ataxias during the final year of her neurology residency training at UCLA. She continued the biochemical research during a neuromuscular fellowship at UCLA and then as a member of the faculty, but also began to treat patients as head of the ataxia clinic. In the last two decades she has seen nearly 4,000 patients with various forms of inherited and non-inherited cerebellar disease – the disorder that causes ataxic symptoms – and currently treats approximately 400.

Given the similarities between ataxias and Huntington's disease and the potential benefits of an ataxia drug she was studying at the time she joined the UCLA faculty, Dr. Perlman also got to know Huntington's disease patients and their families and to build that practice. She now follows close to 200 patients with Huntington's disease, playing a role similar to that with her ataxia patients: making the diagnosis, doing genetic counseling, providing symptomatic treatment and working with the national Huntington's Disease Study Group in designing and conducting trials for new disease-modifying therapies.

The majority of patients with one of the progressive genetic ataxias end up using a wheelchair. In the worst cases, patients develop severe problems with their hands, with speech, and with swallowing, which can be life-threatening. The story is much the same for people with Huntington's disease – a slow, steady progression for 15-20 years, first affecting mobility and, in late stages, potentially causing severe speech and swallowing problems. For Huntington's, though, there is the added insult that mood and behavior can be affected, with some patients developing severe psychiatric symptoms.

Through most of Dr. Perlman's career, there has been precious little to offer these patients. But there are finally reasons to be hopeful. For both Huntington's disease and ataxia patients, a long list of drugs have been used to treat symptoms, all prescribed off-label, with limited effectiveness. Then last August, the U.S. Food and Drug Administration licensed Xenazine (tetrabenazine) for the treatment of chorea (the jerky, involuntary movement) in Huntington's disease – the first treatment of any kind to be approved in the United States for a neurogenetic movement disorder. Meanwhile, the Huntington's Disease Study Group is exploring agents that might be effective in slowing or stop-

Perlman portrait: Mark Berndt

At the age of 9, Brianne Konanz was diagnosed with Friedreich's ataxia, but the effects of the neurodegenerative disorder haven't stopped Konanz, now 31, from enjoying an active life that includes skydiving, river rafting and sit-down skiing. UCLA's Dr. Susan Perlman, her neurologist, is hopeful about new treatments being designed based on a better understanding of the disease.

ping the progression of the disease, and Dr. Perlman hopes these new strategies will be advancing to clinical trials in the coming year.

Dr. Perlman is also the principal investigator at UCLA of an international Phase III trial of the drug Idebenone for patients with Friedreich's ataxia. Idebenone is a modified version of a nutritional supplement that works as an antioxidant and is believed to stimulate and protect nerve cells in the cerebellum. Unlike the symptomatic therapies currently prescribed, Idebenone offers hope for affecting disease progression. "Finally, with our molecular genetic understanding of these disorders we are able to design and test drugs that target the mechanism involved in the disease," says Dr. Perlman.

At the same time, Dr. Perlman is a major contributor to the national Huntington's disease database and has received funding herself from the National Ataxia Foundation for the development of a Web-based national ataxia database. "For rare diseases, there are clinical researchers spread throughout the world, most of whom see relatively small numbers of patients," Dr. Perlman explains. "These databases – in which patients can remain anonymous – enable us to combine clinical information so that our findings are more statistically sound." With additional funding, Dr. Perlman hopes to be able to launch the ataxia database in the near future.

For both the databases and the other clinical studies, Dr. Perlman says, the large ataxia and Huntington's disease patient populations have helped to make the efforts possible. Both patient groups are eager to participate in clinical trials, inspired and motivated by Dr. Perlman to help one another through research.

Giovanna (she asked that her last name not be used) belongs to one of many families affected by Huntington's disease that have helped to ensure that UCLA's Huntington's Disease Center for Excellence remains at the hub of clinical research efforts. She and four of her six siblings have tested positive for the gene mutation that causes Huntington's disease. Two brothers died of the disease and two older siblings have symptoms. Giovanna, 58, remains asymptomatic, but the prospect that she may one day suffer from the disease weighs on her every day. "This disease is so overwhelming for families," she says. "Having a place like UCLA where the doctors are all very knowledgeable, the research is state of the art, and they really care about you is critical. It serves as a light for us."

DR. PERLMAN'S CLINICAL EXCELLENCE was recognized when she received the 2007-08 Sherman M. Mellinkoff Faculty Award, presented to a member of the faculty "whose teaching exemplifies that individual's dedication to the art of medicine and to the finest in doctor-patient relationships." The award is considered the highest honor of the David Geffen School of Medicine at UCLA.

"It was amazing, because you have to be nominated by your peers," says Dr. Perlman. "I was quite honored."

But Dr. Perlman leaves little doubt that she would gladly trade all of the accolades for the types of breakthroughs that would improve the lives of her patients.

"For 20 years all I could do was tell my patients there were no cures, try to treat their symptoms, and fill out their disability forms," she says. "With the development of molecular genetic technologies and the ability to identify responsible genes and understand their proteins, in the last decade we have begun to design treatments aimed at the disease itself. I am very optimistic about what lies ahead." ×

ICU of the Future

With state-of-the-art IT, robotics and monitoring equipment at the new Ronald Reagan UCLA Medical Center, the Neurocritical Care Program continues to lead the way. By Dan Gordon

FOR MANY YEARS, UCLA's Neurocritical Care Program has been an international leader in brain monitoring, brain imaging, and the science of coma, brain injury, and other acute neurological diseases. With the state-of-the-art capabilities of the intensive care unit at the new Ronald Reagan UCLA Medical Center, the program's leadership position has moved a giant step forward.

The new hospital's neuro-"ICU of the future" includes several key features that make it stand out, says Paul Vespa, M.D., director of the Neurocritical Care Program.

Monitoring Tools. Equipment for continuous electroencephalography (EEG) brainwave monitoring, pioneered and promoted by UCLA since the early 1990s as an important facet of neurocritical care, is now available at each patient's bedside. "Most ICUs have EKG monitoring for the heart for every patient, but not brain monitoring," Dr. Vespa notes. Beyond that, the new ICU has additional tools for following brain activity that few can match. This includes the ability to monitor brain pressure, oxygen levels, and metabolism, as well as microdialysis monitoring to determine the chemical makeup of fluids in the brain. An imaging center in the ICU allows the program's physicians to conduct MRI and PET scanning of patients.

Information Technology. New software programs enable the physicians in the Neurocritical Care Program to integrate the data they receive from the diagnostic tools. "All of that information is combined in a continuous series of streams that we can use to enhance clinical decision-making," Dr. Vespa explains. He notes that enhanced clinical decision support is the subject of a major push by the National Institutes of Health (NIH). "We have had a head start in developing and routinely using these kinds of tools in our patient care, and they are more sophisticated than anything else that is out there," Dr. Vespa says.

Robotics. Perhaps the most futuristic element of the new ICU is what's called a "telepresence robot," which is used to monitor and treat patients after hours and from remote locations. "A physician can be at home or on the other side of the world and make rounds on patients from any place that has an Internet connection," Dr. Vespa explains. The robot is maneuvered to the patient's

bedside, and through its audio, visual and networking technology the physician can see the patient, talk with the patient and nurse, and guide treatment, all in real time. Dr. Vespa's group is beginning to use the robot to improve care not only at UCLA, but also at neuro ICUs in smaller hospitals in Southern California that can benefit from UCLA's expertise.

Indeed, the program is making an impact on neuro-critical care well beyond the confines of the new ICU. A fellowship program, one of eight in the nation accredited by the United Council of Neurologic Subspecialties, helps to address the significant shortage of neuro-intensivists through training. In addition, the UCLA Neurocritical Care Program receives substantial funding from the NIH for research, and is using the state-of-the-art technology to reveal important new insights that can be used to improve patient care.

Concludes Dr. Vespa: "Our mission is to provide the highest quality of critical care to patients with life-threatening neurologic disease today, while building the tools, through research and education, that will enable future generations to cure these devastating diseases."

Clockwise from opposite page: MRI scanner being lifted into the 6th floor of the Ronald Reagan UCLA Medical Center, CT/PET scanner in the Neuro-ICU complex, patient EEG monitoring in the Neuro Critical Care Unit.

CLINICAL TRIALS

DRUG FOR FRIEDREICH'S ATAXIA UNDER STUDY IN PHASE III TRIAL

AN ORAL DRUG that may slow the progression of the neurodegenerative disorder Friedreich's ataxia (FA) is being offered in a Phase III trial at UCLA as part of an international clinical trial.

The UCLA Clinical Neurogenetics Program (which includes the Ataxia Center and the Huntington's Disease Society of America Center of Excellence) is participating in the trial for Idebenone, which has been shown to reverse the heart disease associated with FA and is hoped to slow the progression of the neurologic features as well.

FA is an inherited, neurodegenerative disorder characterized by progressive loss of balance, coordination, speech, muscle strength, and heart function. It is the most common ataxia in childhood and adolescence, occurring in 1 in 25,000 people between the ages of 6 and 25. Most children with FA require a wheelchair by age 20 and, if heart disease develops, may die by the age of 30. There are currently no approved drugs for the treatment of FA. Rehabilitation strategies provide modest benefits, but have no impact on the progression of this crippling and life-threatening disease.

The Phase III Idebenone study, sponsored by Santhera Pharmaceuticals (Switzerland) Ltd., was created to collect definitive evidence for the efficacy of Idebenone in slowing or reversing disease progression in FA. Idebenone is a drug developed from a nutritional supplement that is an important factor in cellular energy production and a strong anti-oxidant/free radical scavenger. In the study, subjects will be randomly assigned the actual drug or a placebo. The study will last 26 weeks and will be followed by an open extension study, where all participants will receive the actual drug for up to one year.

All participants are also enrolled in the FA Clinical Outcome Measures study, sponsored by the Muscular Dystrophy Association and designed to develop rating scales and biomarkers that will speed up future drug development. There are currently another 10 drugs in the pipeline, several of which could benefit other neurodegenerative diseases in which free-radical toxicity plays a role.

Interested participants for these studies should call the UCLA HD/ATAXIA Clinical Research Program at (310) 794-1225.

UCLA Neurology currently has open clinical trials and research studies in neuro-oncology (brain tumor), Alzheimer's disease, neurotology (vestibular disorders), multiple sclerosis and stroke. A complete listing with contact information is available at www.neurology.ucla.edu. Under the Research tab, select "Clinical Trials" and then click on "Department of Neurology Clinical Trials and Research."

WHY I SUPPORT UCLA NEUROLOGY

ONE DAY in December 2002, I was at Cloverfield Park in Santa Monica, watching my son's soccer game. When the time came to say goodbye to my friends at the game's end, I thought I was having a bad visual migraine – half their faces had disappeared – but I didn't think it was more than that. My friend noticed something was wrong, asked me to talk to her, and when nothing would come out of my mouth she went across the street to the fire station and got an ambulance for me.

I was taken to a hospital in Santa Monica and given a CAT scan, but the doctors didn't know what was wrong, and I was able to talk again. They kept me overnight, and when I woke up in the morning I was paralyzed on my right side. They realized I'd had a stroke, and put me into an ambulance to UCLA. It was a great comfort to know that I was in a place where they knew what was wrong and what to do to help me. I had a blood clot that had caused the stroke. At the UCLA Stroke Center I was treated with a new approach – flooding my brain with blood and causing the smaller vessels around the blocked one to take over its function. It worked.

I feel so lucky that I found my way to one of the best neurology departments in the world. I had no residual problems as a result of the stroke, and didn't need physical therapy. When I imagine spending my life with the damage that a stroke can cause, I am so glad that these brilliant neurologists are working on new and better treatments. One of the things the neurology department is focused on is finding ways to diagnose and help people in other hospitals – people not as lucky as I was. I'm glad I can help them, because it is thanks to their hard work and inspiration that I have the full life that I do.

—Laura Baker

YOU CAN MAKE A DIFFERENCE!

Your donations help to secure the UCLA Department of Neurology's world-renowned status.
You can direct your charitable gift of cash, securities, real estate, art, or other tangibles to meet areas of greatest need under the direction of Dr. John Mazziotta, department chair, or you can direct your gift to specific research, training, laboratory, or recruitment programs. For more information, please contact Director of Development Patricia Roderick at (310) 267-1837, or email proderick@support.ucla.edu.

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