Summer 2015

UCLA Department of Neurology

Partners *in* Discovery

Bedside to Bench to Bedside:

Patient-Driven Novel Therapies for Multiple Sclerosis

Multiple Sclerosis (MS) is an autoimmune and neurodegenerative disease that affects 400,000 people in the United States. Relapsing-remitting MS, the most common form, can result in permanent disabilities such as loss of vision, paralysis, and cognitive problems. Current MS medications, which can cost patients up to $60,000 per year, have succeeded in reducing relapses and slowing the progression of the disease to some degree, but they do not halt the disease.

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Interim Chair's Column

Marie-Françoise Chesselet, M.D., Ph.D.
Interim Chair, Department of Neurology
Charles H. Markham Professor of Neurology
David Geffen School of Medicine at UCLA

"I am constantly amazed and energized by the courage shown by patients and their families when facing these tough disorders and their resilience in optimizing their quality of life through the maximum treatments available to them."

Since ancient times, spring has been heralded as a time of change. This spring, change has also touched the UCLA Department of Neurology with the departure of our chair, John Mazziotta, M.D., Ph.D., to become vice-chancellor of UCLA Health Sciences and dean of the David Geffen School of Medicine at UCLA, a position that will include serving as CEO of UCLA Health System; and my appointment as Interim Chair of the Department. Twenty years ago, Dr. Mazziotta recruited me to UCLA. We had known each other for more than 10 years through our joint involvement with the Hereditary Disease Foundation. It was Dr. Mazziotta who encouraged me to apply for an open position in the UCLA Department of Neurology, then led by Dr. Robert Collins. My move from the University of Pennsylvania to UCLA was a turning point in my career. One of the greatest reasons was because it came with the most wonderful gift of all: an endowed chair established by the late Dr. Charles H. Markham, who joined the neurology faculty in 1956, served as head of movement disorders, and retired as Emeritus Professor of Neurology in 1995.

The Markham chair enabled me to effect changes in my own research program as needed by the constant progress and discoveries in the field, as well as to foster a unique network of collaborations at UCLA. These collaborations attracted significant federal and private funding and led not only to the identification of new genes and environmental factors that increase the risk of developing Parkinson's disease, but also to the elucidation of new mechanisms and the demonstration that several new therapies improve the disease in scientific models—the first obligatory step before clinical trials. Our reputation in the field grew, new investigators joined, and many trainees left to start their own programs. This success is a testimony to the vibrant spirit of collegiality and bold thinking of basic and clinical investigators in the Department of Neurology and their collaboration with other research units at UCLA, and to the transforming power of the generous philanthropy that made it possible.

After many years heading a basic science department, I am delighted that my new role as interim chair of the Department of Neurology will give me an opportunity to nurture the synergy between the laboratory and the clinic, and bench research and patient care that is the hallmark of our department. This is a time of change, but also of continuity, and I am most grateful to all, from staff to program directors, for their warm and generous welcome and their support in fostering the continuing excellence of our department in the coming months.

Spinning For Dollars—And Brain Cancer Research

A reminder that the 3rd Annual Tour de Pier, the unique fundraising event that brings one of the hottest indoor fitness activities—spinning—to the gorgeous outdoors of the iconic Manhattan Beach Pier, is scheduled for **May 17, 2015.** "Tour de Pier has quickly grown into a signature physical philanthropic event, raising $1,000,000 in just two short years," said Heath Gregory, Co-Founder of Tour de Pier and **Uncle Kory Foundation (UKF), one of the event's three beneficiaries and a donor to the UCLA Neuro-Oncology Program led by Dr. Timothy Cloughesy.** "Our goal this year is to raise $750,000 and, with the incredible support of corporate sponsors and committed individuals, we are confident that we will enjoy another successful event in May."

The UKF is a non-profit, tax exempt 501(c)(3) organization inspired by the life of Kory Lewis Hunter. The organization is dedicated to funding brain cancer research, specifically Glioblastoma. "So many people have been touched by cancer and, while much has been done to fund research and wellness, there is still so much more that we can do to raise funds and heighten awareness. We are confident that Tour de Pier will continue to do both," Gregory continued.

Whether you're a solo rider or a team, the fundraising minimum for each bike is $500. For more information, visit TourDePier.com.

"It has been an honor to serve as chair of the Department of Neurology and it is now a great privilege to lead one of the world's finest medical schools and oversee the UCLA Health System"

New Leadership for UCLA Health Sciences and Department of Neurology

Dr. John Mazziotta appointed Vice Chancellor of UCLA Health Sciences and Dean of David Geffen School of Medicine at UCLA; Dr. Marie-Françoise Chesselet named Interim Chair of Department of Neurology

John C. Mazziotta, M.D., Ph.D.

The Department of Neurology could not be more proud that on March 1, its longtime chairman, John C. Mazziotta, M.D., Ph.D., became vice chancellor of UCLA Health Sciences and dean of the David Geffen School of Medicine at UCLA, a role that includes serving as CEO of UCLA Health System.

"It has been an honor to serve as chair of the Department of Neurology and it is now a great privilege to lead one of the world's finest medical schools and oversee the UCLA Health System," said Dr. Mazziotta. "UCLA is my home. I was a resident and fellow here and completed both my neurology and nuclear medicine training at UCLA. All these perspectives have given me a clear view of what a unique and extraordinary institution and community we have here."

In addition to serving as chair of the Department of Neurology since 2002, Dr. Mazziotta, who joined the UCLA faculty in 1983, has served as associate vice chancellor for health sciences and executive vice dean of the David Geffen School of Medicine since 2012. He has directed the Ahmanson-Lovelace Brain Mapping Center since 1993 and held the Stark Chair in Neurology until his new appointment.

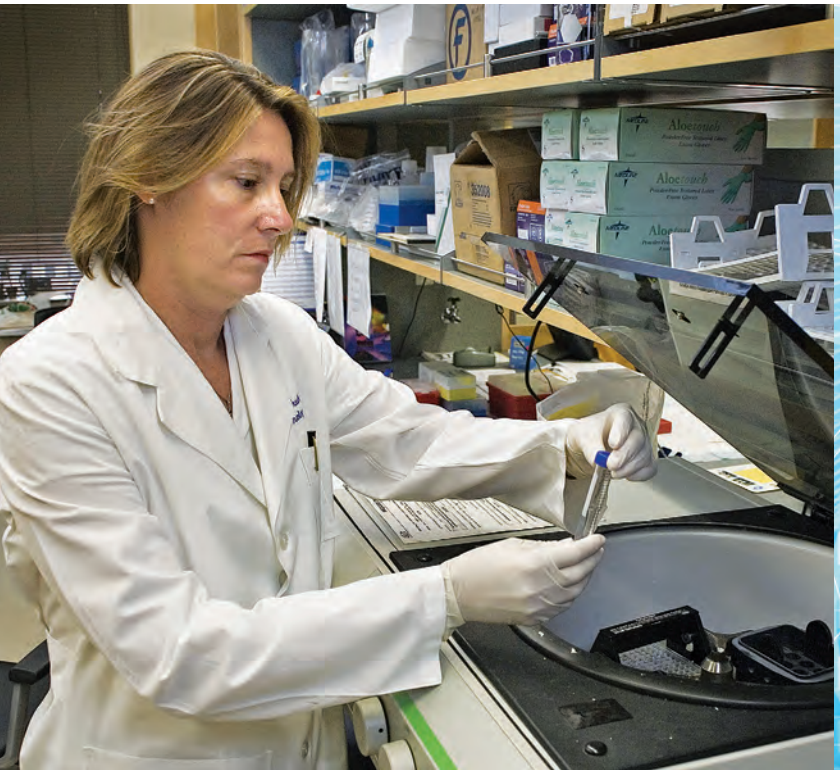
The UCLA Department of Neurology is the second largest in the world. Under Dr. Mazziotta's leadership, the Department grew from 76 to 139 faculty members and achieved the distinction of being first in National Institutes of Health research funding for nine consecutive years. An expert in brain imaging, Dr. Mazziotta established the Brain Mapping Center, which offers all of the methods available to study human brain structure and function. He was the principal investigator of the International Consortium for Brain Mapping, the goal of which was to develop the first atlas of the human brain, including behavioral, demographic, imaging and genetic data from thousands of people.

An effective, accomplished and widely respected faculty administrator with a deep commitment to excellence in education, research, clinical care and public service, Dr. Mazziotta received his bachelor's and master's degrees from Columbia University, and his M.D. and doctorate in neuroanatomy from Georgetown University in 1977. He completed an internship at Georgetown prior to joining UCLA.

"It is a high priority for me to turn over the Department of Neurology to a strong, capable and visionary leader. With this goal in mind, the university has formed a search committee that has launched an international search for qualified applicants for this position. They hope to move forward quickly in identifying, screening, interviewing and recommending the candidates," Dr. Mazziotta said.

In the meantime, the Department is in good hands. Marie-Françoise Chesselet, M.D., Ph.D., long-standing member of the faculty in the Department of Neurology, will serve as Interim Chair until the appointment of a permanent chair.

"This Department has such a strong foundation. I am honored to be stewarding it and I look forward to ensuring a seamless transition," Dr. Chesselet said.



Rhonda Voskuhl, M.D., Ph.D.

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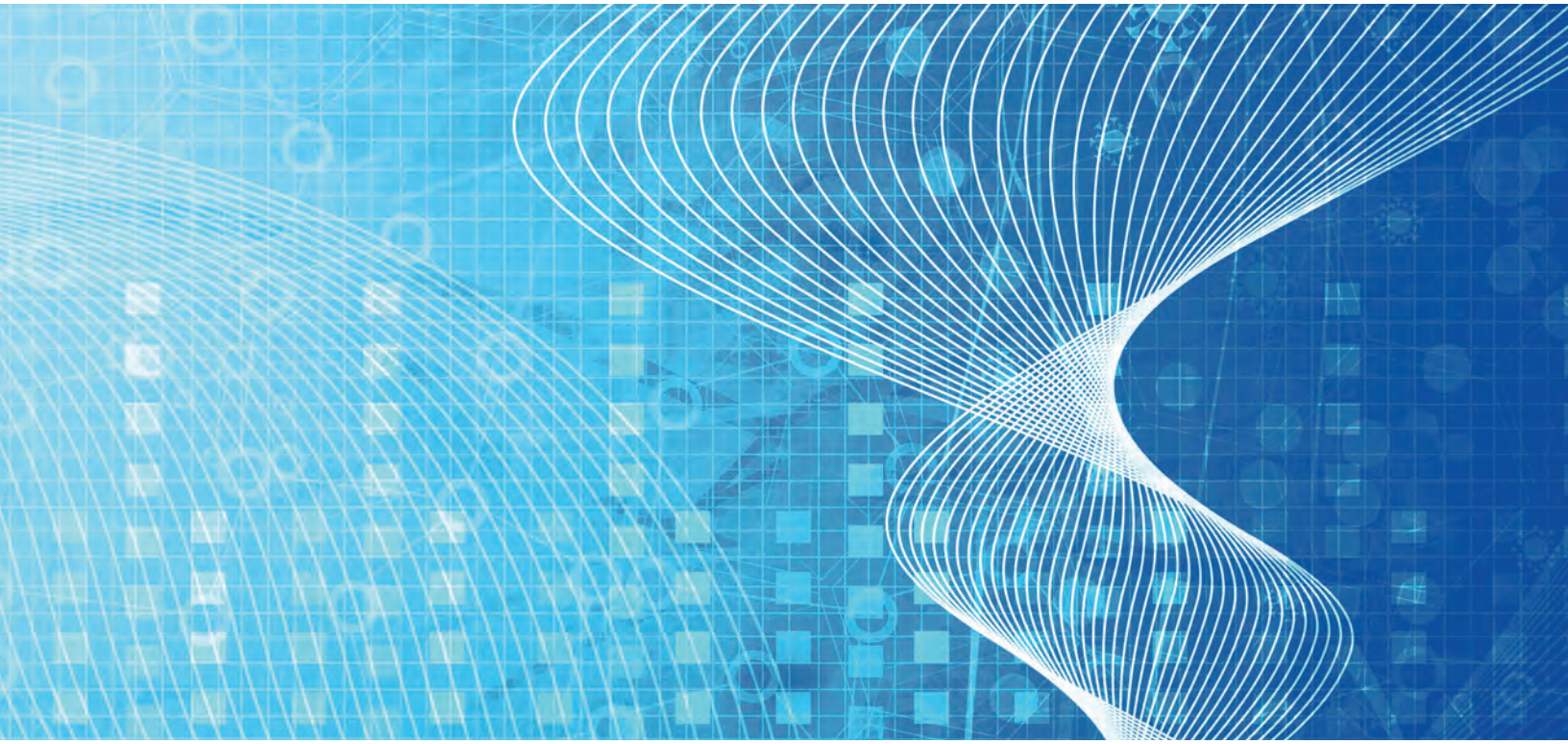
"My approach is different. Over the last 20 years, my research has been focused on patients' observations, not on a molecule or a gene or a technique. Rather, it is based on an understanding of what makes the symptoms of the disease better or worse."

An internationally recognized expert in MS, UCLA neurologist Rhonda Voskuhl , M.D., Ph.D., director of the Multiple Sclerosis Program at UCLA and Jack H. Skirball Chair in MS Research, aims to develop new treatments for the disease through novel therapeutic trials—beginning at the bedside rather than the bench. What makes the program, and Dr. Voskuhl's approach, unique is the latter's three-pronged nature. The epitome of translational research, it starts at the bedside with years of clinical observations that she takes to her lab—the bench—where she does whatever is needed to fix the problem, and then takes it back to her patients. Hence, bedside to bench to bedside.

"Research scientists love to clone molecules and genes," Dr. Voskuhl says, "My approach is different. Over the last 20 years, my research has been focused on patients' observations, not on a molecule or a gene or a technique. Rather, it is based on an understanding of what makes the symptoms of the disease better or worse."

For example, pregnancy is known to make MS relapses decrease by 75 percent, according to Dr. Voskuhl. "That is based on a well known clinical observation. At the bench, we figured out that there was a female hormone, estriol, which could replicate the effect in non-pregnant women. We did clinical trials and reduced relapses."

Indeed, a randomized, double-blind, placebo-controlled trial at multiple sites across the United States and conducted by Dr. Voskuhl showed that combining estriol with Copaxone, a medication currently used to treat MS, reduced the relapse rate by nearly 50 percent with only one year of treatment. In addition, the study showed that women taking both drugs scored higher on cognitive tests after one year than did the women who took Copaxone and a placebo.



The good news is that estriol is a natural biologic, based on a naturally occurring substance, and it has an established safety record, although not yet approved by the FDA. Used for years in Europe and Asia as a hormone replacement therapy for women with menopausal symptoms, it can be given as a pill rather than as an injection, as MS medications are, and it also offers the opportunity for generic pricing, making it more accessible to patients. According to Dr. Voskuhl, the big challenge of doing research based on clinical observations is that the result may not be patentable; thus, most drug companies may not be interested. "New molecules, genes, and techniques are very profitable," she explains.

Another clinical observation that Dr. Voskuhl took to the bench is that men are less likely to get MS; the disease occurs in females at a ratio of three to one. She says that there are all kinds of possibilities for why this happens, including low hormone levels and sex chromosome differences. Yet, men who get the disease have a more rapid progression. Dr. Voskuhl deduced that testosterone might be beneficial. "There is evidence of that at the bench, and we went to clinical trials using a testosterone gel, trying to boost testosterone levels in men with MS." In a small study, in which her team gave testosterone to men with MS to increase their blood levels of testosterone to the high normal range, she found a 67 percent reduction in the brain atrophy rate as well as an improvement in cognitive test results. "We are now hoping to do a larger follow-up, placebo-controlled study with multiple (25) sites across the U.S."

"Both estrogen and testosterone can have neuroprotective effects. Estrogen is also anti-inflammatory, which means patients get two benefits, an anti-inflammatory to reduce attacks and a neuroprotective to ensure that the brain suffers less damage in case of an attack," Dr. Voskuhl explains. "But with both drugs, we're taking something that we know is clinically significant and relevant to people with MS, trying to figure it out, and ultimately taking it back to the bedside in the form of clinical trials."

Dr. Voskuhl says that there is a downside to all the genetic and molecular advances of the last few decades. "All this technology truly reveals the complexity of these diseases and the human body. There are so many genes and molecules and tools to detect and manipulate them, that it's a kind of needle-in-a-haystack approach that can lead to research that is not clinically relevant. With gene arrays, cytokine analysis, and high throughput screenings, there is the likelihood of choosing the wrong gene or the wrong molecule. It's high-risk research. New techniques and screening methods may not replicate the human body."

"My lab does not waste money on research that is not relevant to MS patients," she says. "I am not married to one molecule, but I am committed to fixing Multiple Sclerosis. While we will never find a one-size-fits-all cure, we will find a neuroprotective treatment to halt disabilities. That's where we're going."

According to Dr. Voskuhl, the highly innovative projects of the UCLA Multiple Sclerosis Program owe much of their early success to philanthropy. "To get these projects started, we need private partners. Our earliest stage research is very unique and cannot be funded through traditional means. Later, once there are promising results, we can take them to the National Institutes of Health (NIH) and National Multiple Sclerosis Society (NMSS) for additional funding. The philanthropists who continue to fund our unique approach are our partners in finding a cure for MS. I am deeply grateful to them and, most of all, to our MS patients for allowing us to take this journey with them."

Seeing Inside the Brain

Roger P. Woods, M.D.

Brain imaging has revolutionized the diagnosis and care of many neurologic disorders in recent decades, with millions of diagnostic brain scans performed every year in the United States and around the world. The majority of these scans are performed to screen for abnormalities such as tumors, bleeding, strokes, inflammation and scarring that are detectable in the images by the neuro-radiologist's and neurologist's trained eyes. However, these routine clinical applications only scratch the surface of what can now be achieved by ever more sophisticated brain imaging instruments and analysis methods. Researchers in UCLA's Brain Mapping Program are focused on cutting-edge applications of brain imaging techniques, using them not only to study disease, but also to characterize the function of the normal healthy brain as it develops, matures and ages. Utilizing research-dedicated scanners located in the Ahmanson-Lovelace Brain Mapping Center and computational facilities located in the nearby Neuroscience Research Building, Brain Mapping faculty members and their colleagues from multiple departments across the UCLA campus look daily into living human brains to better understand their function and response to disease.

Magnetic Resonance Imaging (MRI) is the imaging technique used most frequently in the Brain Mapping Program. MRI uses magnetic fields and radio waves to generate brain images. Since it does not use X-rays, MRI can be used to study even children and babies without safety limits on the number of times that a given research subject can be studied. By carefully tailoring the timing and strength of the magnetic fields and radio waves, it is possible to create images that reflect different aspects of brain anatomy, brain blood flow or brain chemistry. Through a generous contribution from the Ahmanson Foundation, the Brain Mapping Center recently upgraded its most frequently used MRI scanner, attaining state-of-the-art capabilities not available on other commercially available scanners. The upgrade allows the magnetic fields to be varied more rapidly and across a wider range and allows signals from the brain to be collected more efficiently. These improvements are particularly important for detailed studies of how different regions of the brain connect and interact with one another, a topic of rapidly growing research interest that is likely to find its way into routine clinical practice in the future.

The Brain Mapping Center has two additional MRI scanners, one that uses weaker magnetic fields and another that uses even stronger magnetic fields to create images. The scanner with the weaker magnetic fields is well-suited for studies of patients who have had brain implants for the treatment of disorders such as Parkinson's disease, since the U.S. Food and Drug Adminstration has recently approved scanning of such patients using lower strength magnetic fields. Brain Mapping Center faculty members have prioritized studies of neuromodulation using implanted devices or using non-invasive strategies such as transcranial magnetic stimulation (TMS) or direct current stimulation (DCS) as a major ongoing research focus. The MRI scanner with the stronger magnetic field is not large enough for scanning whole human brains but can be used for post-mortem scanning of brain sections. The technology to scan living humans using these stronger magnetic fields is under development, and Brain Mapping faculty have a collaborative arrangement with the Beijing MRI Center for Brain Research in China that affords access to one of these high-magnetic field human instruments.

In addition to MRI scanners, the Brain Mapping Center also has a positron emission tomography (PET) scanner. PET scanners make brain images using very small amounts of radioactivity that are injected into the subject or patient. Depending on the chemical that the radioactivity is attached to, PET scanners can make precise measurements of blood flow, energy consumption, the quantities of proteins on cell surfaces that respond to signals from other cells, or substances such as amyloid, which accumulate in diseases such as Alzheimer's disease. The availability of PET and MRI scanning within a single facility simplifies studies that seek to make use of both types of scanning, as well as studies designed to evaluate newer MRI techniques that might become suitable future replacements for current PET techniques.

As MRI and PET instruments become more sophisticated, they generate ever larger amounts of data showing ever finer degrees of detail. Brain Mapping faculty have developed techniques to account for differences in the size and shapes of brains to create brain atlases and to identify subtle differences or changes in the brain. Such differences can distinguish individuals with disease from healthy individuals or can characterize changes in response to disease progression or treatment. Brain Mapping faculty members also produce software tools that are used world-wide for collecting, analyzing and visualizing brain images. For studies that involve hundreds or even thousands of participants, supercomputing capabilities well beyond what can be achieved by current desktop machines are needed. Although housed in a different building, the Brain Mapping Program's supercomputing facilities have a direct fiber optic connection to the Ahmanson-Lovelace Brain Mapping Center, providing seamless and rapid communication between the scanning instruments and the supercomputing power needed to fully interpret the scans.

Across several decades, progress in brain imaging has provided ever improving windows for seeing inside the living brain to understand brain structure and function in health and in disease. The breadth and depth of UCLA's clinical neurological populations, together with a vibrant neuroscience research community, complement the state-of-the-art imaging equipment and expertise available within the Brain Mapping Program, paving the way for ever better windows in the decades to come.

Meet Our Fellows

Adrienne Keener, M.D.

Dr. Adrienne Keener in front of the Parthenon in Athens, Greece

A first-year fellow in movement disorders, Dr. Adrienne Keener completed her residency in Neurology at UCLA and served as chief resident last year. "I really enjoyed residency and medical school education," she says. "When I was a junior resident working at the West Los Angeles VA, Dr. Jeff Bronstein was the attending physician. He asked me if I had thought about what I wanted to do. I realized that Movement Disorders was a really great fit for me, and I'm grateful that he allowed me to stay for fellowship."

A graduate of UC San Diego and University of Southern California's Keck School of Medicine, Dr. Keener was inspired to study the brain by a personal experience. "My grandmother had Alzheimer's disease," explains the Bay Area native. "I studied cognitive science in college and found working with patients with neurologic illness to be both stimulating and rewarding."

Passionate about patients and clinical care, during her residency Dr. Keener found that she wanted a long-term, lasting relationship with patients. "I want to be able to help them navigate the ups and downs. I like the clinical variety in movement disorders, and diagnosing and treating these patients is truly an art."

Dr. Keener will stay at UCLA for a second year of fellowship. "In the second year, I look forward to having more time to explore opportunities for research," she says.

One of Dr. Keener's research interests is in developing tools to predict how patients will respond to certain therapies. She is curious about working with Dr. Bronstein to study the genetic and environmental interplay in patients with Parkinson's disease.

In addition to patient care, Dr. Keener is interested in medical education and the integration of humanities and medicine. "I'm interested in narrative medicine, which is really using storytelling as a tool to explore the patient/physician relationship. I think this helps physicians develop skills to communicate and empathize with their patients. It can also provide a creative outlet for both patients and physicians. For example, some patients find that keeping diaries is therapeutic to their illness."

Dr. Keener and her husband are both physicians. They met in medical school and were thrilled to match together at UCLA. He is completing residency in general surgery.

NEW CLINICAL TRIAL FOR THOSE AT RISK FOR ALZHEIMER'S DISEASE

Dr. Kathleen Tingus, Director of the Neuropsychology Clinic in the Department of Neurology and Associate Director of Operations of the Mary S. Easton Center for Alzheimer's Disease Research at UCLA, has been actively involved in clinical services, teaching, and numerous clinical trials investigating Alzheimer's disease treatments since 1999. "The number of patients with this disease has grown rapidly in recent years. We are hoping to slow the progression of the disease with therapeutic agents," she explains. "Our goal is to intervene before the onset of significant cognitive losses with early drug intervention."

Dr. Tingus performs neuropsychological evaluations of patients who present with cognitive complaints, and quantifies the level of cognitive and functional impairment in order to help neurologists refine their differential diagnoses. These evaluations are designed to assess the patient's cognitive performance in the domains of attention, memory, language, spatial skills, and executive functioning, as well as assess for changes in behavior, mood, and motor functioning. "I am typically seeing these patients at a very vulnerable point in their lives," Dr. Tingus says. "The testing process can be challenging for patients, as we are tapping

Kathleen D. Tingus, Ph.D.

Director, Neuropsychology Clinic, UCLA Department of Neurology

Associate Director of Operations, Mary S. Easton Center for Alzheimer's Research at UCLA

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

into areas of weakness and cognitive decline. It is an honor for me to walk with them through this process and to help provide diagnostic clarification and answers to challenging questions. Sometimes the most difficult phase is not knowing what the patient is facing. We provide clarification and assist families and patients in coping with difficult diagnoses."

Currently, Dr. Tingus is working with the Anti-Amyloid Treatment in Asymptomatic Alzheimer's study (the "A4" study), which is testing a new investigational treatment, called an anti-amyloid antibody. The hope is that this can slow memory loss caused by Alzheimer's disease. Scientists believe that a buildup of amyloid (a protein in the brain that can build up in older people) deposits may play a key role in the eventual development of Alzheimer's disease-related memory loss. The overall goal of the A4 study is to test whether decreasing amyloid with antibody investigational treatment can help slow this memory loss in some people.

Participants in the study are older individuals (ages 65-85) who have normal thinking and memory function, who may be at risk for memory loss due to Alzheimer's disease, but have no outward signs of the disease. The study seeks to enroll 1,000 adults who have an elevated level of amyloid plaque in their brains. Positive emission tomography (PET) scans will be used to determine evidence of this plaque buildup in potential participants.

The three-year A4 study is a landmark public-private partnership sponsored by the National Institute on Aging/NIH, Eli Lilly and Company, and several philanthropic organizations. The A4 trial is coordinated by the Alzheimer's Disease Cooperative Study.

Dr. Tingus also serves as the director of the UCLA Alzheimer's Disease Research Center (ADRC) Neuropsychology practicum training program and has mentored more than 100 Ph.D. students over the past 18 years.

UCLA One of 12 Sites for Clinical Trials for Spinal Muscular Atrophy Drug

Spinal Muscular Atrophy (SMA) is a severe and rare genetic neuromuscular disease that affects the motor neurons (nerve cells) in the spinal cord. Characterized by muscle weakness, atrophy, and progressive degeneration, SMA is the number one genetic cause of death in children under the age of 2. Babies with SMA are not able to hold up their heads, roll over, crawl, and sit up or walk without support. Children with SMA grow weaker as their disease progresses.

Now there is hope for these young patients and their families. Currently, UCLA is a site of two Phase 3 clinical trials, ENDEAR (for infants) and CHERISH (for children), for this devastating disease, says Perry Shieh, M.D., Ph. D., Professor of Neurology at the David Geffen School of Medicine at UCLA. The studies are sponsored by Isis Pharmaceuticals, Inc.

ENDEAR is a 13-month study in approximately 111 infants diagnosed with SMA. CHERISH is a 15-month study in approximately 120 children between the ages of 2-12 with SMA who are non-ambulatory. The study will evaluate the efficacy and safety of a dose of ISIS-SMNRx delivered into the spinal fluid via a lumbar puncture every four months.

"Children with SMA have a mutation of the SMN1 gene," says Dr. Shea. "It doesn't work." The drug ISIS-SMNRx is designed to alter the splicing of a closely related gene (SMN2) to increase production of fully functional SMN protein, which is deficient in SMA patients and the same protein that is made from SMN1. While it is not a cure, the drug is most likely to slow deterioration and progression of the disease, the severity of which correlates to the amount of SMN protein.

One in 50 people, the equivalent of about 6-million people in the United States, are carriers of a defective SMN1 gene, which is unable to produce fully functional SMN protein. According to Dr. Shieh, infants with Type I SMA, the most severe form, produce next to no SMN protein and have a life expectancy of less than two years. Children with Type II have greater amounts of SMN protein but still have a shortened lifespan and cannot stand independently. Children with Type III have a normal lifespan but experience lifelong disabilities. Carriers experience no symptoms and do not develop the disease.

"This landmark study is the first that has held this kind of promise," says Dr. Shieh. UCLA is one of only 12 sites in the United States where the drug is being tested, and the only site in Southern California. The U.S. Food and Drug Administration granted orphan drug status and fast track designation to ISIS-SMNRx to treat all types of SMA.

Why I Do This

Dr. Mollie Johnston and her husband at their wedding in Greece

Dr. Mollie Johnston

Director, Clinical Operations
Headache and Interventional Pain
UCLA Headache Research and Treatment Program

> "It is so rewarding. This is something I never thought would be possible in any other area of neurology. Patients get instantly better."

"I see a lot of patients with migraines who have been to 30 doctors and tried hundreds of pills," says Dr. Mollie Johnston, Director of Clinical Operations, Headache and Interventional Pain, UCLA Headache Research and Treatment Program. Dr. Johnston, a specialist in interventional pain management, performs interventional headache procedures on patients who don't respond to drugs or who experience too many side effects from them. She has discovered a new protocol—a radiofrequency technique—treating upper cervical nerve roots in the neck to relieve pain patterns at the front of the eye or the base of the skull. Basically, the 15- to 20-minute treatment modulates pathways from the back of the head to the forehead, suggesting that those nerves are connected or are more sensitive in patients with migraine.

"I found by accident that C1 stimulation triggers eye pain," Johnston says. "I started with a three-needle protocol in the C1, C2 and C3 levels to treat occipital (upper neck) pain and found that in migraine patients, C1 can treat pain around the eye. Radio frequency ablation at the C1 level by heating the nerve can reduce migraine for up to 10 months. We now have research going on with UCLA Radiology to see if there is an anatomical correlate to this or if it is just sensitization that occurs during migraine."

The discovery was published in the *Annals of Neurology* in 2013. Dr. Johnston has presented lectures on the procedure at the American Headache Society, the International Headache Society, and at the European Headache and Migraine Treatment International Congress (EHMTIC), the premier international event for experts and healthcare professionals with an interest in migraine and headache disorders.

"It's a huge discovery," she says. "It suggests that interventions in migraine patients need to target C1, which is a nerve that was previously thought to lack a role in pain or sensation."

Dr. Johnston explains that, while it took a year to be able to do the technique in a safe and medically sound way, she has been getting referrals from as far away as Hawaii, New York, Florida, South Carolina, and Texas, as well as from all over California. UCLA is currently the only place doing the highly technical procedure.

"It is so rewarding. This is something I never thought would be possible in any other area of neurology. Patients get instantly better. The procedure is safe, effective, and patients don't have to keep cycling through medications with side effects that can be as crippling as the pain itself," she says. "Whether the headaches are genetic or hormone-related and whether they are triggered by stress, the weather, altitude, or hormones, patients often need an intervention to get them out of the cycle of pain when medications fail. This procedure offers patients improved quality of life, and hope. That's why I do it."

Volunteer Faculty

Kolar N. Murthy, M.D.

Volunteer faculty member Dr. Kolar Murthy (Narasimhamurthy) teaches general neurology to UCLA neurology residents at the West Los Angeles Medical Center, which is part of the VA Greater Los Angeles Healthcare System. He teaches about a third of the students there. "I like teaching, I've been doing it for so long—almost 43 years," says the alumnus of the UCLA Neurology Training Program, who ran the VA's Multiple Sclerosis clinic for six years before leaving in 1977 to go into private practice. "Years ago, all the students used to come to the VA for the Introduction to Neurology Clinic, but now that's all done on the Westwood campus."

"Despite the technological explosion in medicine, I like clinical, patient-oriented teaching, where you present a case and take off from there," he says, explaining that as a medical student, he was inspired by a neurologist who demonstrated findings. "At that time, there was no CT scan or magnetic resonance imaging (MRI). Clinical exams were precise and 'mathemagical,'meaning diagnosis appears like magic when neurological examination is followed in a mathematical way. Now we have the support of technology, but everything still begins with the patient. You must come to a reasonable conclusion before ordering tests."

Dr. Murthy grew up in South India and received his medical degree from Mysore Medical College. He came to Chicago for his internship and laughs that one year there was enough. He completed his residency in Internal Medicine at UC Irvine.

Early on, Dr. Murthy was impressed by neurology more than any other specialty. "Even from my med school days I wanted to be a neurologist," Dr. Murthy says. "I am old-fashioned. I like to examine patients, to get their histories. This is experience- and evidence-based neurology. I like to draw conclusions from the examination."

Dr.Murthy retired from private practice a year ago and now teaches general neurology on a volunteer basis at the VA Long Beach Healthcare System in addition to UCLA. He also teaches didactic classes at UC Irvine.

MEET
A
SCIENTIST

Dr. Varghese John

From left: Jesus Campagna, Dr. Varghese John, Dr. Barbara Jagodzinska, and Patricia Spilman

"As the population ages, the development of new drugs is critical, especially for CNS disorders such as Alzheimer's disease, Parkinson's disease, ALS and brain tumors"

Dr. Varghese John is an accomplished medicinal chemist, a drug discovery specialist, and a pharmaceutical industry veteran. He holds a Ph.D. degree in Medicinal Chemistry from the University of Minnesota and completed two postdoctoral fellowships in laboratories of renowned chemists—at the University of Chicago with Dr. Josef Fried, and at Stanford University with Dr. Carl Djerassi.

As a faculty member in the Mary S. Easton Center for Alzheimer's disease Research, directed by Dr. Dale E. Bredesen, Dr. John leads the Drug Discovery & Translational Laboratory in the Department of Neurology at UCLA. His lab focuses on small molecule drug discovery, comprising screening to discover validated hits, performing hit-to-lead optimization, and conducting lead profiling and preclinical studies to select drug candidates that possibly can be translated from the bench-to-bedside.

"As the population ages, the development of new drugs is critical, especially for CNS disorders such as Alzheimer's disease, Parkinson's disease, ALS and brain tumors,0" Dr. John says. "But it is an arduous and expensive process to develop drugs targeting the brain. We need to find small molecules that can cross the blood brain barrier, or develop technologies—such as is being done in the lab using microfluidics—that allow for ferrying molecules to the brain."

Previously Dr. John served with the Buck Institute for Research on Aging, Athena Neurosciences, and Elan Pharmaceuticals, where he led a team of medicinal chemists developing drugs for diseases of the central nervous system (CNS) with a focus on Alzheimer's disease (AD). His work at Elan included the development of potent inhibitors for two key enzymes involved in the formation of the Aß peptide and amyloid plaques found in the brains of AD patients.

Dr. John is an inventor, with more than 100 pending or issued patents on compounds and analogs for CNS-related targets. He says that an academic medical institution such as UCLA is an exciting place to be right now, as it has many aspects of the drug discovery process already in place, and provides opportunities to collaborate with outstanding researchers. His goal is to develop a pharmaceutical industry model in UCLA's academic research setting.

Dr. John's current research is in the development of therapeutics for AD and other neurodegenerative disorders. The focus of his AD research includes: (1) the discovery of small molecules that increase the levels of a trophic fragment affected in AD. A candidate from this class, F03, has advanced into Phase 2 clinical trials in Australia, for subjects with mild cognitive impairment due to AD. According to Dr. John, F03 performed extremely well in the preclinical AD models. "It looks and behaves like a promising drug for AD. We'll find out for sure soon, and then we hope to conduct an additional clinical trial here at UCLA"; (2) the discovery of molecules that target ApoE4, the major genetic risk factor in AD, and thus delay the onset of the disease in people with this risk factor; (3) the discovery of APP-selective ß- secretase inhibitors that could prevent disease pathology; (4) the discovery of corticotrophin-releasing factor (CRF) receptor modulators that reduce p-Tau and reverse memory deficits; and (5) the discovery of molecules that inhibit the neurotoxic intracellular APP-C31 cleavage.

Dr. John says it is important to point out that drug discovery is truly a team effort and he is proud to be working with a great team comprising Patricia Spilman, M.A.; Barbara Jagodzinska, Ph.D.; Tina Bilousova, Ph.D. and Jesus Campagna, M.S.

Crystal Ball for a Cure Advances Neuromuscular Research

Top: David Nygaard & his employees Bottom: Doug Earlenbaugh and family

From ornate peacocks to ghosts, the costumes at the Crystal Ball for a Cure are as diverse as the people whose lives have been touched by neuromuscular disease. Fifteen years ago, when her 15-year-old son was diagnosed with Muscular Dystrophy, Linda Fox-Jarvis founded Crystal Ball for a Cure Inc., a non-profit organization dedicated to raising funds to support studies in Muscular Dystrophy. Proceeds from the organization's elegant annual fundraising event help advance the research of UCLA scientist Melissa Spencer, Ph.D., who has dedicated her life's work to conducting innovative investigations in limb-girdle muscular dystrophy type 2A. This disease causes progressive muscle weakness and many patients eventually become wheelchair bound. Philanthropic support is crucial to advancing the science. The Department of Neurology extends sincere thanks to Linda and her organization. Visit www.crystalballforacure.com to be part of the magic this Halloween in Virginia Beach, Virginia.

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ART OF THE BRAIN
UCLA NEURO-ONCOLOGY PROGRAM

Save the Date

Mark your calendars for Saturday evening, September 26, 2015. That's when we celebrate Art of the Brain's 16th Annual Gala at UCLA's Schoenberg Hall. Guests will pay tribute to the courageous men and women facing brain cancer and honor the unforgettable individuals sadly lost. Art of the Brain celebrates their talent and joie de vivre with a festival of gourmet food and wine, special performances and opportunities to win fabulous prizes. Please join us as we celebrate "The Art of Friendship".

Art of the Brain, founded by Judi Kaufman, has a mission to raise public awareness of brain cancer, raise money for the UCLA Neuro-Oncology Program, and spotlight the talent, strength and courage of brain cancer patients.

For more information, please call (310) 825-5074. www.artofthebrain.org

Judi Kaufman and her grandson

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MEET
OUR
ALUMNI

From left: Dr. Andrew Woo, son Miles (15), wife Gina and son Julian (12)

Andrew Woo, M.D., Ph.D.

Alumni of the UCLA Department of Neurology utilize their training in a variety of different ways. While many treat patients, others apply their expertise to research and academic medicine.

"The brain is so pure, it's the one area where you can diagnose by verbal and physical exam," explains Dr. Andrew Woo, who has a private neurology practice in Santa Monica. "Think of the neurologist as the detective at the bedside."

A graduate of Cornell University, Dr. Woo received his medical degree from the Warren Alpert Medical School of Brown University, where he also earned a Ph.D. in neuroimmunology. After his internship at New York Presbyterian/Weill Cornell Medical Center, he completed his residency in neurology at UCLA, followed by a fellowship in clinical electrophysiology at Harbor-UCLA Medical Center. Although Dr. Woo elected to go into private practice, he is on the clinical faculty of UCLA and allows medical students and residents to rotate through his office in Santa Monica. In addition, he is in charge of Board review for neurology residents at UCLA and Cedars-Sinai Medical Center. "It keeps me on my toes," he explains.

The neurology landscape has changed completely since Dr. Woo completed his specialty training in 1996. Then, there was only one FDA-approved treatment for MS. There are soon to be 13. It was his Ph.D. research into how the brain communicates with the immune system that inspired him to specialize in the treatment of MS. "The brain regulates vocabulary. How does the brain affect coordination, agility, balance, and speed? How does it affect muscle memory?"

A music and martial arts aficionado, Dr. Woo served on the Shotokan karate team at Cornell and now studies Brazilian Jiu-Jitzu. He wonders how the brain trains the body to do these things. He plays the trombone professionally in jazz, funk, and salsa bands and has played with Tito Puente, Joe Henderson, and in concert at Carnegie Hall. Again, he relates music to the brain: how does the brain develop integrative patterns to create jazz—that 'glorification of the inexact?'

"There was a unique thing about training at UCLA," he says. "As a resident, you have clinic patients who look to you as their doctor. For three years of training, it's as if you run your own practice. It's a lot of responsibility, but you get to work with renowned professors within their clinics and their specialties and have the benefit of their great minds. It's a kind of big buffet and you learn how to approach patient exams in all these different clinics. This was a luxury that was not offered by other neurology programs."

"There is also the fact that everyone is warm and friendly," Dr. Woo adds. "UCLA Neurology has a family feel. All the residents are close."

Dr. Woo puts his medical knowledge to extracurricular use. He has served as medical consultant on the first season of "House," the pilot for "Night Shift," and as a musician for "The Bonnie Hunt Show."