CHAIRMEN’S MESSAGE

Stanford’s commitment to collaborative multidisciplinary research among our faculty and our strong clinical partnerships with referring physicians—regionally, nationally and internationally—foster world-class patient care and exceptional outcomes.

This Neuro-Innovation issue highlights our novel collaborative model and defines the future of neuroscience at Stanford.

Our clinical and research programs combine the strengths of Stanford Hospital & Clinics and Lucille Packard Children’s Hospital (LPCH) to deliver world-class patient care. Over 130 full-time School of Medicine neurology and neurosurgery faculty and affiliated hospital-based faculty provide comprehensive neuroscience clinical services. Propelled by Northern California’s burgeoning population, Silicon Valley technology, and extraordinary School of Medicine and Hospital leadership, major expansion is underway of both Stanford Hospital & Clinics and LPCH that will transform patient care in the 21st century (www.sumcrenewal.org).

This issue features our unique partnership between Stanford and local affiliates, exemplifying our focus on collaboration as we mobilize experts in acute and chronic traumatic brain injury, including specialists in rehabilitation and epidemiology, to improve care and outcomes for polytrauma patients.

We also showcase our pioneering multigenerational model for patients with complex diseases of the peripheral nerves and muscles. Specialists at Stanford Hospital & Clinics and LPCH work together to treat patients over their lifespan in a newly renovated state-of-the-art outpatient Neuromuscular clinic for adult patients.

In October 2012, Stanford Stroke Center received the nation’s first Comprehensive Stroke Center certification by the Joint Commission. Our neurologists, neurosurgeons, neuroradiologists, nurse specialists, basic scientists and clinical researchers, led by our original founders, provide the most advanced complex stroke care possible. We are proud of our multidisciplinary team that achieved this tremendous milestone.

Underscoring our dedication to excellence from bench to bedside, Stanford scientists continue to demonstrate exciting results, such as small-molecule therapeutics and naturally occurring brain proteins that reduce the effects of stroke and stimulate functional recovery in animal models. These discoveries have translational potential as future stroke therapeutics. Over 70 international basic and clinical neuroscientists and rehabilitation specialists joined us at our inaugural 2012 Spinal Cord Injury Symposium to advance the field of regenerative medicine in spinal cord injury. The new Jill and John Freidenrich Center for Translational research is a state-of-the-art hub for the multiple clinical trials we have underway and include in this issue of Neuro-Innovation.

We are committed to our partnerships with referring physicians and look forward to your inquiries at 1.800.800.1551. We welcome opportunities to collaborate with you on basic research, clinical trials and patient care as we strive to make a positive difference in every patient’s life.

We invite you to join us November 1–2 for the 2013 Breakthroughs in Neurologic Therapies CME course in San Francisco, California, for our latest clinical and research updates.

Frank M. Longo, MD, PhD
George E. and Lucy Becker Professor
Chairman, Department of Neurology and Neurological Sciences

Gary K. Steinberg, MD, PhD
Bernard and Ronni Lacroute-William Randolph Hearst Professor of Neurosurgery and the Neurosciences
Chairman, Department of Neurosurgery
INSIDE THIS ISSUE
1 CHARMEN'S MESSAGE
2 STROKE CENTER
   Nation’s First Comprehensive
   Stroke Center Certification
   Breakthrough in Hunt for Stroke Therapeutics
4 NEUROSPINE PROGRAM
   Excellence Spans the Continuum of Polytrauma Care
   Neurospine and Orthopaedics
   Forge Collaboration
   Potential First in Class Treatment for Spinal Cord Injury
6 NEUROMUSCULAR PROGRAM
   Regeneration Reporter Mouse
   Comprehensive Clinic for Neuromuscular Disorders
8 CLINICAL TRIALS
   Stanford Opens State-of-the-Art Clinical Trials Center
12 NEW FACULTY
14 GENETIC PROGRAMS
   Innovative Neurogenetics Program
   Exemplifies Partnership
15 REFERENCES

STROKE CENTER

Nation’s First Comprehensive Stroke Center Certification

The Stanford Stroke Center, established in 1992 as one of the first multidisciplinary centers of its kind, was the nation’s first recipient of the Comprehensive Stroke Center Certification in 2012, awarded by The Joint Commission. The multidisciplinary team of complex stroke care specialists is honored to be recognized with the highest level of center certification.

As a global leader in stroke research and treatment, the Center has received a number of awards for clinical excellence and has provided care for more than 25,000 patients with cerebrovascular disorders. In addition, consistently ranking as one of the most prolific research groups in the nation, Stanford has developed major advances in medical therapies, neurosurgical techniques and interventional neuroradiology procedures.

The Neurocritical Care Program has made key advances in the diagnosis of intracerebral hemorrhage and prognosis of coma. Stanford neuroscientists have helped clarify the basic mechanisms of stroke-induced brain injury and have pioneered several new imaging techniques.

The three visionary founders of the Center are still actively innovating and leading cutting edge complex stroke care. “The Stanford Stroke Center’s foundational philosophy is key to its success,” says Center director Greg Albers, MD. “To partner neurosurgery, neurology and interventional neuroradiology seemed sensible,” he adds, “but it was a unique concept then. We were confident that this approach would be fruitful, and the administrators at Stanford Hospital and the University supported us.”

Over 50 hospitals initially applied for the certification, involving a rigorous review process.

Breakthrough in Hunt for Stroke Therapeutics

αB-crystallin breaks ΠA’s treatment window barrier

In a recent study led by Gary Steinberg, MD, PhD, and Lawrence Steinman, MD, the George A. Zimmermann Professor of Neurology and Neurological Sciences and of Pediatrics, mice treated with αB-crystallin—a naturally occurring anti-inflammatory found by Dr. Steinman to reduce brain inflammation in animal models of multiple sclerosis—demonstrated reduced infarct sizes even when administered up to 12 hours after stroke. This is well beyond the 4.5 hour treatment window of the only approved drug for stroke, tissue plasminogen activator (tPA).

This groundbreaking work, published in PNAS14, has important implications as tPA can only dissolve blood clots, whereas αB-crystallin interferes with the post-stroke inflammatory processes that contribute to brain damage and thus may offer a therapeutic role. Co-first authors Ahmad Arac, MD, and Sara Brownell, PhD, found that mice engineered to lack αB-crystallin experienced worse infarcts and more brain inflammation, and that reintroduction of αB-crystallin into these deficient mice significantly reduced lesion sizes. αB-crystallin treatment in wild-type animals also decreased the ability of certain immune cells to secrete deleterious molecules in the post-stroke brain. Of note, plasma levels of αB-crystallin were elevated in mice after stroke and in human stroke patients—especially in younger patients, whose recovery from stroke is often accelerated, though not in patients older than 80 years, whose strokes are often more catastrophic. Future studies aim to confirm these results and test extended time-windows as well as optimal dosing.

Small molecule enhances post-stroke recovery

Stanford researchers, led by senior author Marion Buckwalter, MD, PhD, assistant professor of neurology and neurological sciences, and neurosurgery, are applying small molecule therapeutics to post-stroke recovery. Their promising results, recently published in Stroke, show that a small molecule designed to target one of two receptors on neurons for brain-derived neurotrophic factor (BDNF) can stimulate the birth of new neurons from the brain’s resident stem cells and improve functional recovery in adult mice after ischemic stroke. This molecule, called LM22A-4, showed efficacy even when administered didn’t start until 3 days after stroke onset. This means that the compound, rather than limiting stroke’s initial damage, enhanced recovery. The experimental mice, trained in maneuvers before undergoing stroke, were administered daily doses of LM22A-4 for 10 weeks starting at post-stroke day 3 and had their motor skills tested. All showed significant functional improvement over their non-treated counterparts. Importantly, LM22A-4 administration also doubled the numbers of new mature and immature neurons adjacent to the stroke-damaged area of the brain.

Interdisciplinary Team. This collaboration encourages networking and discussions that are valuable because of their frankness.

Stroke is the fourth leading cause of death and the most common cause of adult disability. More than 795,000 strokes occur in the United States each year; as the population ages, it is estimated that the number of strokes will increase substantially over the next decade. During the Center’s third decade, even more dramatic breakthroughs are anticipated in stroke research. Stanford’s clinical, educational, and research programs continue to innovate and the tremendous support the Center has received from the community is greatly appreciated.
Excellence Spans the Continuum of Polytrauma Care

Odette Harris, MD, MPH, treats acute traumatic brain injured patients as well as subacute and chronic patients in her role as associate chief of staff, polytrauma, and director of Defense Veterans Brain Injury Center at the Veterans Affairs Palo Alto Health Care System Polytrauma System of Care (VAPACHS PSC). This gives her a unique opportunity to think upstream and downstream in terms of enhanced outcomes for her polytrauma patients.

Most trauma departments are compartmentalized. “Traditionally we briefly see the patients and their rehab specialists after surgery,” she says, “but in this new model we can see how effective our methods are across a continuum of care and communicate with our embedded neuropsychology and physical medicine and rehabilitation colleagues.”

A unique partnership between the VAPACHS, Stanford and Santa Clara Valley Medical Center (SCVMC) brings data together from experts treating a wide range of civilian, veteran and active duty patients with a lifetime of follow-up care. At the forefront of clinical standards, with a world-class trauma team supported by a network of subspecialties in rehabilitation and epidemiology, these Stanford partnerships inform the field by contributing to guidelines in severe traumatic brain injury (TBI) across the entire disease matrix.

Dr. Harris, associate professor of neurosurgery and director of brain injury, is also involved with the ProTECT II clinical trial examining the therapeutic potential of progesterone in TBI. Dr. Harris points to her colleague Greg Goodrich, PhD, whose research with collaborators led to a national directive mandating vision screening for all TBI patients.3

The TBI research forum on March 15 created a unique networking experience across all levels of expertise.4 Stanford’s innovative atmosphere continues to attract world-class experts with essential qualities of authenticity, ethics, passion and hard work who then partner to develop trust and ask each other “How are you changing the world?”

MARK YOUR CALENDAR!

Join the Stanford Neurosciences faculty in beautiful San Francisco for this dynamic conference.

November 1-2, 2013
Location: JW Marriott, Union Square, San Francisco, CA
For more information visit: cme.stanfordhospital.org

Neurospine and Orthopaedics Forge Collaboration

At Stanford neurosurgeons and orthopaedic surgeons share their highly specialized skills.

From the Biostatistics and Health Research and Policy departments, have recently been awarded a prestigious grant from the Orthopaedic Research and Education Foundation; one of only five in the nation, titled “Developing a patient-centered clinical tool for assessment of risk of perioperative complications in spine surgery procedures.”

Dr. Ratliff highlights the partnership that Graham Creasey, MD, professor of neurosurgery and the Paralyzed Veterans of America Professor of Spinal Cord Injury Medicine, spearheaded between Stanford, SCVMC, the VAPACHS and other regional institutions to provide the commercial infrastructure and unparalleled research environment necessary for spinal cord injury clinical trials. It is difficult to pull all the required components together for a complex clinical trial site as was the case for the Geront stem cell trial. Stanford’s dedicated infrastructure accelerates the pace of research, fosters innovation and advances therapeutic development. With open dialogue between world-class surgeons and a wide spectrum of interdisciplinary researchers, the future is bright for NeuroSpine at Stanford.

Potential First in Class Treatment for Spinal Cord Injury

In a major breakthrough, LM11A-31 promotes functional recovery in a mouse model of spinal contusion injury. This non-peptide small molecule demonstrated the ability to cross the blood brain barrier following oral administration, as well as the blood spinal cord barrier, without toxic effects. The study, a collaboration between Frank Longo, MD, PhD, professor and chair of neurology and neurological sciences, and colleagues from The Ohio State University, University of California at San Francisco and Stanford University, was recently published in The Journal of Neuroscience.5 Administered beginning 4 hours after injury, and twice daily thereafter, CNS/plasma levels were exceptionally favorable. Improved motor behavior, especially gait and overall coordination, was observed. Spinal cord injury leads to death of oligodendrocytes and loss of myelin. LM11A-31 administration led to a twofold increase in the number of spared oligodendrocytes and an accompanying increase in myelinated axons (see figure), an effect similar to that seen following cell transplantation after spinal cord injury (SCI).

This novel, noninvasive, mechanism-based therapeutic blocks proN

The Journal of Neuroscience

Vehicle LM11A-31

Following spinal cord injury there is a loss of myelinated axons (left). Treatment with LM11A-31 leads to sparing of myelinated axons (right).

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Regeneration Reporter Mouse

In both the clinic and laboratory, Thomas Rando, MD, PhD, professor of neurology and neurological sciences, has devoted his career to the study of muscle diseases, in particular the muscular dystrophies caused by mutations in the dystrophin gene (Duchenne muscular dystrophy), the caveolin-3 gene (limb-girdle muscular dystrophy 1C) and the dysferlin gene (limb-girdle muscular dystrophy 1B). Dr. Rando studies skeletal muscleature to understand the biology and genetic mechanisms involved in homeostasis and disease states while building models toward novel therapeutics.

There is still no cure or effective therapy for muscular dystrophies, only temporizing interventions such as corticosteroid use, surgical tendon release and assisted ventilation. While these interventions may improve the quality and length of life in some patients, Dr. Rando believes the discoveries necessary to advance truly beneficial therapies for patients depend on animal models that reflect human disease progression.

An exciting recent study from Dr. Rando's laboratory is reported in Journal of Clinical Investigation.1 Lead author Katie Maguire, PhD, and colleagues created a successful mouse model of limb girdle Muscular Dystrophy 2B that safely and non-invasively tracks dystrophic disease progression over time. They call it the “regeneration reporter” mouse. This mouse model vastly improves on standard histological analysis of muscle. The reporter model allows real-time quantitative monitoring of disease progression in a living animal over time with bioluminescent imaging of muscle stem cells, specifically, that express the luciferase gene. When the stem cells proliferate in response to muscle degeneration caused by the disease, luciferase expression increases.

The regeneration reporter mouse in this study was monitored over 18 months. Dr. Rando and his group found that clinical disease progression strongly correlates with increases in bioluminescent signals in this dystrophic model. Moreover, onset of disease can be detected before it is histologically evident. This technology is also applicable to all murine models of muscular dystrophy. The future of regenerative medicine and preclinical evidence of disease rests on outcomes such as these.

Dr. Rando sees this model, to be shared with researchers around the globe, as an extremely effective noninvasive tool to test potential therapeutics. He believes that sharing data with other researchers leverages Stanford's expertise and accelerates the clinical translation of laboratory discoveries.

“Stanford is such a rich environment for collaboration,” Dr. Rando says, “there is an exceptional colleague around every corner and the opportunity to apply state-of-the-art technology to translate basic laboratory research into clinically relevant advances.” With regard to these kinds of studies, Dr. Rando points to the value of facilities such as the Richard M. Lucas Center for Imaging, which is devoted to research in magnetic resonance imaging (MRI), spectroscopy (MRS) and computed tomography (CT) imaging and a collaborative model by design, that offers state-of-the-art imaging technologies for studies ranging from basic biology to clinical therapeutics.

Comprehensive Clinic for Neuromuscular Disorders

John W. Day, MD, PhD, has expanded upon the transitional care model often used in diseases like cystic fibrosis to a visionary modality he calls family-based treatment.

One family exemplifies the importance of this new approach. The youngest member of the family was born with severe generalized weakness that resulted in inadequate breathing, requiring a tracheostomy and full-time mechanical ventilation for the first 9 months of life. Further complicating her development, her weakness interfered with her ability to speak or use sign language. Even though these severely weak patients are often deemed hopeless, and support is withdrawn, with awareness of recent evidence that this patient’s strength would improve, both she and her mother (several family members having been shown to be affected) received optimal, aggressive, multidisciplinary support (initially with Dr. Day and other providers outside California, but now at LPCH and Stanford Hospital Neuromuscular Clinic); the patient, now 6 years old, is ambulatory, breathing without tracheostomy or ventilator support, and mainstreamed in school, where she is doing extremely well. Clearly family-based support and up-to-date information on disease progression and management can significantly affect outcome.
Comparison of overall survival post-\textit{CyberKnife} radiosurgery treatment of patients with 1-3 versus 4 or more brain metastases
Pt: Steven D. Chang, MD
Co-Pt: Judith A Murawc, MD, Griff Harsh, MD, Gordon Li, MD, Je C. Gibbs, MD, Scott Saltys, MD, Steven Hancock, MD
(NCT01778764)
\textbf{CyberKnife Radiosurgery and Quality of Life}
Pt: Steven Chang, MD
(NCT01165329)
A Phase II Study of Rindopepimut/GM-CSF in Patients with Relapsed EGFRVIII-Positive Glioblastoma
To determine if adding the experimental vaccine rindopepimut (also known as Czik 110) to bevacizumab can slow tumor growth and improve progression-free survival of patients with relapsed EGFRVIII positive glioblastoma.
Pt: Gordon Li, MD
(NCT01498328)
Effects of Growth Hormone on Cognition and Cerebral Metabolism in Adults
To elucidate the effects of growth hormone replacement in patients with growth hormone deficiency on cognitive function using structural and functional neuroimaging and cognitive testing.
Pt: Laurence Katznelson, MD
(NCT01007071)
A Phase I/II Study of Vorinostat Concurrent with Stereotactic Radiosurgery for Trigeminal Neuralgia
Pt: Clara Choi, MD, PhD and Scott Saltys, MD
(NCT01364259)
A Phase I/II Trial of Fractionated Stereotactic Radiosurgery to Treat Large Brain Metastases
To determine the optimal radiation dose.
Co-Pt: Scott Saltys, MD and Clara Choi, MD, PhD
(NCT01059226)
A Phase I/II Trial of Temozolomide and Hypofractionated Radiotherapy in the Treatment of Supratentorial Glioblastoma Multiforme
To determine the safety and effectiveness of 1 week versus 6 weeks of hypofractionated radiotherapy in combination with temozolomide.
Co-Pt: Scott Saltys, MD and Clara Choi, MD, PhD
(NCT01120839)
A Study of Patient Reported Outcomes After Stereotactic Radiosurgery for Trigeminal Neuralgia
Pt: Clara YH Choi, MD, PhD and Scott Saltys, MD
(NCT01364285)
Investigation of DTI MRI as a Correlate to Pain Relief and Facial Numbness in Patients Following Stereotactic Radiosurgical Rhizotomy for Trigeminal Neuralgia
Pt: Clara Choi, MD, PhD and Scott Saltys, MD
(NCT01364272)
Prostatectomy for the Treatment of Traumatic Brain Injury (ProTECT III)
To determine if intravenous [IV] prostatectomy, started within 4 hours of injury and given for a total of 96 hours, is more effective than placebo for treating victims of moderate to severe traumatic brain injury.
Stanford Pt: Jim Quinn, MD
Sub-Pt: Marco Lee, MD
(NCT00822930)
A Study of Amifostine for Prevention of Facial Numbness in Patients Receiving Stereotactic Radiosurgery for Trigeminal Neuralgia
Co-Pt: Clara Choi, MD, PhD and Scott Saltys, MD
(NCT01364259)
A Phase I/IIA Study of the Safety and Efficacy of Modified Stromal Cells for spinal metastases
Pt: Steven Chang, MD
(NCT01165329)
A Study of Amifostine for Prevention of Facial Numbness in Patients Receiving Stereotactic Radiosurgery for Trigeminal Neuralgia
Co-Pt: Clara Choi, MD, PhD and Scott Saltys, MD
(NCT01364259)
To investigate the long term safety, tolerability, and efficacy of ACT-126800 (Ponesimod) in patients with relapsing remitting Multiple Sclerosis
Pt: Jeffrey Dunn, MD (NCT01093026)

An Extension Protocol for Multiple Sclerosis Patients who Participated in Previous Studies of Alentuzumab
Pt: Jeffrey Dunn, MD (NCT00980553)

Biobank For MS And Other Demyelinating Diseases
To establish a large, longitudinal collection of high quality samples and data from subjects with MS, selected other demyelinating diseases as a shared resource to scientists researching the causes, sub-types, and biomarkers of MS and related demyelinating diseases.
Pt: Jeffrey Dunn, MD (NCT01044387)

Prognostic Value of MRI and Biomarkers in Comatose Post-cardiac Arrest Patients (COMA)
To assess the value of state-of-the-art brain imaging techniques (MRI), and blood tests in predicting outcome in these patients.
Co-PI: Greg Albers, MD, and Karen Hirsch, MD
Pt: Lawrence Recht, MD (NCT01093459)

Phase 1 Study of MABT5102A on Brain Amyloid and Related Biomarkers in Patients with Mild to Moderate Alzheimer's Disease (BLAZE)
A randomized trial of healthy older adults to assess effects of innovative activities on remediation of age-related cognitive decline.
Pt: Victor Henderson, MD (NCT01094509)

A Phase II Trial of MBT5102A on Amyloid Imaging and Cognition in Alzheimer’s Disease
A randomized trial in patients with mild cognitive impairment and AMY-101 to assess the impact of AMY-101 on brain amyloid and cognition.
Pt: Lawrence Recht, MD (NCT01094327)

Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage Phase III (CLEAR III)
To determine if EVO placement with low-dose rt-PA improves modified Rankin Scale scores at 6 months compared to subjects treated with EVD alone.
Pt: Chitra Venkat, MD (NCT00784134)

Stroke Hyperglycemia Insulin Network Effort (SHINE) Trial
To determine safety and therapeutic benefit of treating hyperglycemic acute ischemic stroke patients with targeted glucose concentration (80mg/dl - 130mg/dl).
Pt: James Quinn, MD (NCT01369069)

The Phase II, Single Arm, Open Label Study of NKR-102 in Bevacizumab-resistant High Grade Glioma
Co-PI: Lawrence Recht, MD and Seema Nagpal, MD (NCT01663012)

An International Study of Rindopepimut/GM-CSF with Adjuvant Temozolomide in Patients with Newly Diagnosed, Surgically Resected, EGFRIv-positive Glioblastoma (ACT IV)
Pt: Lawrence Recht, MD (NCT01482347)

Phase III Study of Vorinostat in Bevacizumab and Low-dose Deferoxamine in Patients with Newly Diagnosed Intracranial Hemorrhage
To determine if EVD placement with low-dose Deferoxamine in patients with spontaneous intracerebral hemorrhage following maintenance Bevacizumab and Temozolomide in newly diagnosed High Grade Glioma.
Pt: Paul Fisher, MD (NCT01365503)

Phase III Study Evaluating Limited Target Volume Boost Irradiation and Reduced Dose Craniospinal Radiotherapy 18.00 Gy and Chemotherapy in Children with Newly Diagnosed Standard Risk Medulloblastoma
Pt: Paul Fisher, MD (NCT00857736)

Comprehensive Molecular Analysis of Tumor Samples Derived From Patients with Diffuse Brainstem Glioma—A Pilot Study
Pt: Paul Fisher, MD (NCT00899834)

Phase II Screening Trial of Temozolomide with Irinotecan versus Temozolomide, Irinotecan plus for Recurrent/Refractory Medulloblastoma/ CNS PNET of Childhood
Pt: Paul Fisher, MD (NCT01217437)

Phase II Clinical Trial Evaluating the Efficacy and Safety of GDC-0449 in Children with Recurrent or Refractory Medulloblastoma
Pt: Paul Fisher, MD (NCT0129316)

Phase III Randomized Trial of Post-Radiation Chemotherapy in Patients with Newly Diagnosed Ependymoma Ages 1 to 21 years
Pt: Paul Fisher, MD (NCT01096308)

Phase II Study of Sunitinib in Recurrent, Refractory or Progressive High Grade Glioma and Ependymoma Brain Tumors in Pediatric and Young Adult Patients
Pt: Paul Fisher, MD (NCT01462690)

Phase II Trial of Response-Based Radiation Therapy for Patients with Localized Central Nervous System Germ Cell Tumors (CNS GCT)
Pt: Paul Fisher, MD (NCT01626668)

Immunologic Profile of Patients with Newly Diagnosed Medulloblastoma at Initial Diagnosis and During Standard Radiation and Chemotherapy
Pt: Paul Fisher, MD (NCT01334749)

A Phase II Placebo-Controlled Trial of Modafinil to Improve Neurocognitive Deficits in Children Treated for a Primary Brain Tumor
Pt: Paul Fisher, MD (NCT01381718)

Migraine Prophylaxis with BOTOX in Children
To study BOTOX (Botulinum Toxin Type A) purified neurotoxin complex for headache prophylaxis in adolescents (children 12 to 18 years of age) with chronic migraine
Pt: Sheena Aurora, MD (NCT0129316)
### NEUROSURGERY

**Jun Ding, PhD**  
Assistant Professor of Neurosurgery  
Dr. Ding studies functional organization of motor circuits in the brain, particularly cortico-thalamo-basal ganglia networks, using electrophysiology, 2-photon microscopy, optogenetics and genetics. He aims to construct functional circuit diagrams and establish causal relationships between activity in specific groups of neurons, circuit function, animal motor behavior and motor learning, as well as help construct psychomotor disorder circuit diagrams for disorders such as Parkinson’s disease.

**Mehrdad Shamloo, PhD**  
Associate Professor (Research) of Neurosurgery and Comparative Medicine and by courtesy of Neurology  
Dr. Shamloo studies the pathology underlying nervous system injury and neurologic disorders, such as stroke, Alzheimer’s disease and autism, focusing on mechanisms that lead to functional and behavioral malfunctions. He uses experimental and transgenic rodent models, in conjunction with experimental therapeutic approaches, such as small molecule therapeutics, to accelerate discoveries into novel treatments. Major focuses are the beta 1-adrenergic receptor and signaling cascade and Npas4, a transcription factor.

**Suzanne Tharin, MD, PhD**  
Assistant Professor, Neurosurgery  
Suzanne Tharin, MD, PhD is investigating the repair of the damaged corticospinal circuitry. She is focusing on mechanisms that lead to functional and behavioral malfunctions. She uses experimental and transgenic rodent models, in conjunction with experimental therapeutic approaches, such as small molecule therapeutics, to accelerate discoveries into novel treatments. Major focuses are the beta 1-adrenergic receptor and signaling cascade and Npas4, a transcription factor.

### NEUROLOGY

**Fahd R. Khan, MD, MSc**  
Clinical Assistant Professor of Neurosurgery  
Dr. Khan practices neurosurgery at the Stanford Neurosurgery Clinic in Los Gatos. His specialty interests include pain management, degenerative spine conditions and movement disorders. He brings extensive training in deep brain stimulation, epilepsy surgery, interventional pain management as well as stereotactic and functional neurosurgery.

**Gerald A. Grant, MD**  
Acting Associate Professor of Neurosurgery  
Dr. Grant is a neurosurgeon-scientist at Lucile Packard Children’s Hospital with clinical interests in pediatric brain tumors, pediatric epilepsy surgery, ChiarI malformations, minimally invasive endoscopy, and endoscopic cranial surgery. Dr. Grant runs a translational brain tumor laboratory focusing on the blood-brain barrier and is investigating novel ways to improve drug delivery into the brain. He also is an Air Force veteran and has a longstanding interest in traumatic brain injury.

### Movement Disorders

**Camilla Kilbane, MD**  
Clinical Assistant Professor of Neurology and Neurological Sciences  
Dr. Kilbane specializes in the evaluation and treatment of movement disorders. She provides comprehensive care for patients, such as patient assessment for unconfirmed diagnoses, second opinions, medication management, neurostimulator adjustments for patients after DBS and botox treatment.

**Karen G. Hirsch, MD**  
Assistant Professor of Neurology and Neurological Sciences and by courtesy of Neurosurgery  
Dr. Hirsch cares for critically ill patients with neurologic disorders in the intensive care unit. Her research focuses on novel imaging techniques such as functional brain imaging in patients with cardiac arrest and traumatic brain injury. She also studies methods of non-invasive measurement of cerebral blood flow, oxygenation, and cerebrovascular autoregulation and how these parameters can be targeted to improve outcome in patients with neurologic injury.

### Neuromuscular Disorders

**Neelam Goyal, MD**  
Clinical Assistant Professor of Neurology and Neurological Sciences  
Dr. Goyal specializes in the diagnosis, management and electrophysiological testing of neuromuscular diseases. Her research interests include ALS and sleep, hereditary neuropathies and neuromuscular junction disorders.

**Pediatric Neurology**

**Katherine Mackenzie, MD**  
Clinical Assistant Professor of Neurology and Neurological Sciences  
Dr. Mackenzie directs Lucile Packard Children’s Hospital movement disorders clinic, focusing on disorders such as dystonia, chorea, tremor, ataxia, tics and Tourette’s Syndrome.

### Neurocritical Care

**Courtney Wusthoff, MD**  
Assistant Professor of Neurology and Neurological Sciences  
Dr. Wusthoff is a neonatal neurologist and co-director of the new Lucile Packard Children’s Hospital Neuro Neonatal Intensive Care Unit. Her research focuses on the use of EEG monitoring in critically ill neonates, to identify those at neurologic risk and guide treatment.

**Brenda Porter, MD, PhD**  
Associate Professor of Neurology and Neurological Sciences  
Dr. Porter is a pediatric neurologist with specialty training in epilepsy. She uses medications, brain stimulation devices, ketogenic diet and surgical approaches to treat a child’s seizures and improve their overall brain health. Her research focuses on improving epilepsy surgery outcomes, novel molecular approaches to prevent epilepsy and understanding the cause of sudden unexplained death in epilepsy.

**Cynthia J. Campen, MD, MS**  
Clinical Assistant Professor of Neurology and Neurological Sciences  
Dr. Campen practices at Lucile Packard Children’s Hospital in child neurology and pediatric neuro-oncology, and is the assistant residency director for Child Neurology. Dr. Campen’s research interests include epidemiology of childhood brain tumors, late effects of brain tumor treatments and intracranial vasculopathy.

### Headache

**Sheena K. Aurora, MD**  
Clinical Assistant Professor of Neurology and Neurological Sciences  
Dr. Aurora specializes in headache disorders and novel treatments for migraines. She is active on several committees and boards and is a national leader in headache research. As lead investigator for the PREempt1 trial Dr. Aurora oversaw approval of BOTOrx for chronic migraines. Her current clinical research efforts involve transcranial magnetic brain stimulation for the treatment of headaches.

**Scheherzade Le, MD**  
Clinical Assistant Professor of Neurology and Neurological Sciences  
Dr. Le is an adult general neurologist with specialty training in epilepsy, electroencephalography and intraoperative monitoring. Her clinical and research interests include tuberous sclerosis and waveform analysis of transcranial motor evoked potentials.

### NEW FACULTY
Innovative Neurogenetics Program Exemplifies Partnership

Dr. Steven Chang had a vision: a clinic with the interdisciplinary complexity to match the needs of patients with neurogenetic disorders who often spend a lifetime navigating medical specialties with various doctors who may have little communication with each other.

Improved outcomes and quality of life for these patients are now a reality at Stanford’s Clinical Neurogenetics Oncology Program, the first program of its kind in Northern California.

Along with his four days a week in clinic, Dr. Chang has an innovative partnership model that is just as likely to see him making outreach visits, with referral forms preprinted in Vietnamese, to a community neurologist’s office as it is to see him leverage Stanford’s electronic medical record technology to send notes to a referring physician as a patient is wheeled to the recovery room.

He believes that soon, through the efforts of the Stanford Neuromolecular Innovation Program (SNIP) research group, these patients will have access to less expensive, minimally invasive testing to screen for neurogenetic biomarkers.

Through the support and commitment of Stanford to the bench-to-bedside approach of personalized medicine, Dr. Chang, professor of neurosurgery and the Robert C. and Jeannette Powell Neurosciences Professor, is able to provide multimodal care to families with incredibly complex needs. The dedicated multidisciplinary team includes specialists in neurosurgery, neurol ogy, neuro-ophthalmology, neuropsychology, neuromuscular radiology, dermatology and genetics who use a patient-centered approach with state-of-the-art services. Personalized treatment plans may include CyberKnife radiosurgery, neurointerventional radiology procedures and neurosurgical interventions.

Coordinated care allows a patient to schedule all appointments with a wide range of specialists in a span of one or two days, thereby ensuring that disease monitoring and management take place with the least difficulty for the family. Communication is essential, so the team actively monitors and makes improvements to this process. A patient can either call or email the clinical care coordinator with symptoms and often be seen the next day. Preprinted forms are available to speed the referral process and the feedback loop is a priority, as Dr. Chang believes that the best partnership is an equal one between Stanford and referring physicians. He is often on the phone with referring physicians for updates on their patients, and feels this goes a long way to honoring the relationship already established before the referral.

“We are here to act as a backstop, providing support and filling in the gaps with our specialty expertise,” he says, “and we absolutely respect the trust a patient has developed with their referring doctor.” The Clinical Neurogenetic team has extensive expertise in handling the most complicated cases. These include autosomal recessive diseases, such as hereditary hemorrhagic telangiectasia, and autosomal dominant diseases, such as neurofibromatosis (NF) Type 1 & Type 2, schwannomatosis, Von Hippel-Lindau (VHL) disease, tuberous sclerosis and Sturge-Weber syndrome.

Stanford has the longest institutional experience with CyberKnife and VHL and has been named a Clinical Care Center of Excellence by the VHL Family Alliance.

Partnerships with other national support groups include the National Acoustic Neuroma Association and the Neurofibromatosis Network. Many of these patient support networks hold their regular meetings at Stanford.

Data collected from lifetime monitoring are essential to the research in the SNIP laboratory, and to Lori Shoemaker, PhD, who was recruited by Dr. Chang and Dr. Steinberg to lead this basic science research effort at Stanford.

The laboratory currently focuses on two rare cerebrovascular diseases—brain arteriovenous malformations (AVMs) and Moyamoya disease (MMD). Research in this field is challenging as there are currently no suitable animal models for these two diseases, so Dr. Shoemaker’s research is based entirely on human samples, including blood and tissue obtained during surgery.

The support of patients and their families in this effort is crucial to advancing knowledge of these diseases, understanding what causes them and learning how to better diagnose and treat patients with AVMs and MMD.

Using existing human cell lines in culture is also an important research tool for testing hypotheses, as is shown in the image of human endothelial cells forming vessel-like tubes in culture. Dr. Shoemaker recently discovered that human brain AVMs acquire abnormal expression of proteins that are usually associated with lymphatic vasculature. As the brain does not normally have a lymphatic system, this may have the potential to change the way the underlying basic disease biology is understood.

The research and clinical groups are currently working together to develop translational approaches to understand what these basic research advances mean to patients and their treatment and outcomes, including their risk of hemorrhage.

To refer adult patients to any Neurosciences service at Stanford please call 650.723.6469.

MD Help Line
1.866.742.4811
Transfer Center/LifeFlight
1.800.800.1551

REFERENCES

Stroke Center

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Science Writers/Editors
Greta L. Boekhuls and Cindy H. Samos
Design
Nicole Dacunno and Vivian Libert
Fusion of muscle cells to generate “Differentiated myotubes” in a model of mature muscle cells.

Image provided by Thomas Rando, MD, PhD, Stanford professor of neurology and neurological sciences.