Neurosurgery Active Research Projects, July 2008

Qilin Cao, MD

- Enhancing Remyelination as a Mechanism for Spinal Cord Repair
  The major goal of this project is to test if a combinatory strategy, including blocking inhibitory Notch signaling, increasing expression of growth factor D15A, and transplantation of OPCs will promote remyelination and facilitate functional recovery after spinal cord injury.
  Funded by NIH/NCRR
- Combinatory Strategies to Functional Remyelination after Spinal Cord Injury
  The goal of this grant is to examine the roles of active astrocytes on remyelination and to identify the optimal strategies to promote remyelination and functional recovery after the demyelinated and contused injury in rats.
  Funded by NIH/NINDS
- Dr. Cao is setting up the Mission Connect Center at The University of Texas Health Science Center at Houston where he will explore the therapeutic utility of oligodendrocyte-restricted precursor cells, a type of stem cell, to treat people with spinal cord injury.
  Funded substantially by Mission Connect Foundation.

Peng Roc Chen, MD

- A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA)
  The objective of the study is to determine whether medical management compared to interventional therapy (with endovascular procedures, neurosurgery, or radiotherapy, alone or in combination) improves the long term outcomes of patients with unruptured brain arteriovenous malformations (BAVM). The secondary objective is to compare the impact of medical management to interventional therapy with respect to adverse events, quality of life and cost. In this prospective, multicenter, parallel design, randomized, controlled trial, both groups are receiving medically approved treatments for this disease. The experimental part of this study is that the choice of treatment will be made by random assignment rather than by the patient or the doctor. Patients with an unruptured BAVM without prior interventional therapy and with no contraindications to interventional therapy will be candidates for this trial. Patients will be followed for a minimum of 5 years and a maximum of 7.5 years from randomization.
  Funded by Trustees of Columbia University, New York City

Guy L. Clifton, MD

- National Acute Brain Injury Study: Hypothermia IIR
  This is an important multi-center trial to determine the effects of early cooling on patients with severe traumatic head injury. The purpose of the study is to determine if the induction of moderate hypothermia early after injury in patients aged 16-45 will result in an increased number of patients with good outcomes

compared to patients randomized to normothermia.
Funded by NIH

- Anterior Cervical Fusion Outcome
  The objective of this study is to evaluate the outcome of patients after anterior cervical fusion with plating. Specific aims include evaluation of patients' neck pain before and after surgery and documentation of the anterior fusion rate following anterior cervical fusion surgery.
  Funded by Aesculap, Inc.

John W. Crommett, MD

- North American Clinical Trials Network for the Treatment of Spinal Cord Injury, "The Network" (NACTN)
  The NACTN Registry's goal is to document the routine care and the course of the injury for spinal cord injury patients. This is done through a network of clinical centers collecting standardized de-identified data from patients presenting with a new traumatic spinal cord injury (SCI). Information will be collected on the natural history of SCI and course of treatment through the first 12 months following the date of injury. Data collected includes imaging information from CT or MRI scans, neurological and general medical outcome and rehabilitation evaluation. A secondary objective is to be one site of a network prepared to collaborate on interventional/observational trials for treatment of spinal cord injury
  Funded by Christopher Reeve Paralysis Foundation
- Phase I Trial of Riluzole in Patients with Acute Spinal Cord Injury (Part of NACTN Network)
  The aim of this Phase I clinical trial is to evaluate safety and provide preliminary efficacy data related to the use of riluzole in patients with acute traumatic spinal cord injury. The trial will collect information about efficacy outcomes in SCI subjects treated with riluzole.
  Funded by Christopher Reeve Paralysis Foundation and Department of Defense

Pramod Dash, PhD

- Proteomics of Brain-Trauma-Associated Elevated Intracranial Pressure
  One of the major causes of death following brain trauma is increased intracranial pressure (ICP). Currently, there are no effective ways to predict if the ICP of a patient will reach uncontrollable levels. Various cytokines (balance between pro-and anti-inflammatory) and other factors are thought to underlie increases in ICP. In a translational study we are comparing protein patterns found in the blood of traumatic brain injury patients with those of healthy volunteers. The specific aim of the PROTEOMICS study is to determine if the serum from brain-injured patients contains reproducible protein markers that appear prior to elevations in ICP.
  Funded by NIH, Mission Connect, and Center for Clinical and Translational Sciences

Timothy Ellmore, PhD

- Hemispheric Laterality Predicted by Structural Connectivity
  Surgery to cure severe epilepsy requires that brain areas important for producing and understanding language be identified. Language function is typically organized such that one hemisphere of the brain is dominant. The gold-standard method for identifying the dominant hemisphere involves an injection of sodium Amytal into the carotid artery to temporarily render one hemisphere non-functional while language tasks are administered to assess speech production. This procedure is risky and costly. This research project seeks to determine hemispheric dominance in epilepsy patients using high resolution non-invasive imaging of brain structural connectivity and function with the ultimate goal of replacing the invasive sodium Amytal procedure.
  Funded by Epilepsy Foundation

Raymond Grill, PhD

- Spatial and Temporal Blood-Spinal Cord-Barrier Dysfunction in Chronic Spinal Cord Injury
  The goal of this grant is to explore the significance of failure of spinal cord vasculature in the chronic phase of injury. Such loss of vascular integrity may indicate the presence of long-term pathological processes previously thought to be restricted to the acute phase of injury.
  Funded by TIRR Foundation/Mission Connect
- Phosphodiesterase-inhibitors, Vascular Integrity and Spinal Cord Injury
  The goal of this research is two-fold: 1) to investigate repair and/or stabilize spinal vasculature in the acute phase of spinal cord injury using phosphodiesterase inhibitors to improve outcome and 2) to begin to understand the pathological factors that contribute to vascular dysfunction in the chronic phase of spinal cord injury.
  Funded by NIH/NINDS
- Inflammation in Chronic Spinal Cord Injury
  This study's objective is to determine the role of arachidonic acid-derived mediators in inflammation and how they contribute to the pathology observed in the chronic phase of spinal cord injury.
  Funded by Paralyzed Veterans of America
- Mission Connect Mild TBI Translational Research Consortium
  The overall goal is to develop new interventions in the treatment of mild traumatic brain injury through a multi-institutional collaborative effort. Dr. Grill's specific component of the project is to provide a core facility for the processing and image analysis of brain tissue samples provided by other consortium members.
  Funded by the Department of Defense
- MRI of Angiogenesis in Spinal Cord Injury
  The goal of this project is to utilize non-invasive MRI methods to study vascular repair following spinal cord injury.
  Funded by NIH/NINDS
- Use of PC-NSAIDs in a Rodent Model of Chronic Central Pain

This study's goal is to determine whether chemically-modified non-steroidal inflammatory drugs can improve both locomotor and neurosensory function following spinal cord injury.
Funded by Department of Defense/Army

Georgene Hergenroeder, MHA, RN

- Biomarkers for Pain in Spinal Cord Injury
  The objective of this study of biomarkers in patients with spinal cord injury is to identify molecular markers in blood plasma that are linked to chronic pain. The goal is to isolate biomarkers that identify patients at risk for the development of neuropathic pain. In future studies these markers will be targeted for therapeutics. The ultimate goal is to use molecular markers to identify patients at risk for developing chronic pain in order to intervene early in the process to preserve normal function as long as possible or to prevent the onset of chronic pain and the morbidity associated with chronic pain.
- Proteomics of Brain-Trauma-Associated Elevated Intracranial Pressure
  Co-investigator with Pramod Dash, PhD
- Neuroscience Research Repository (NRR)
  In order to expand neuroscience research and move laboratory advances to patients, there is a need to integrate reliable clinical data with biologic information from patient tissue specimens. The Neuroscience Research Repository was established to meet this need. It is a database and tissue sample bank that collects and stores information and samples for current and future neuroscience research. Its objective is to make data and tissue samples available for study of neurological conditions. The large volume of patients with neurological trauma and illness who are treated by Department of Neurosurgery generates an extensive amount of data and samples that are valuable for scientific research.
  Funded by the Vivian L. Smith Center for Neurological Research

Dong H. Kim, MD

- Identification of Coding Variants Associated with Cerebral Aneurysm Pathogenesis
  The long-term goal of this project is to identify gene defects that may contribute to the development of cerebral aneurysms, to understand the pathogenesis of cerebral aneurysms at the molecular level, and to increase the ability to identify individuals at risk. The study aims to identify families affected by cerebral aneurysms and families affected by both cerebral aneurysms and aortic aneurysms; to perform genetic linkage analyses in cerebral aneurysm families; and to identify genetic mutations involving the coding regions. Another aim is to characterize the association between identified TGFB (transforming growth factor beta, a growth factor synthesized by skeletal cells) receptor variants and cerebral aneurysm patients.
  Funded by American Stroke Association-Burgher Foundation Centers for Stroke Prevention Research (Collaboration with Harvard-Burgher Center)

Nobuhide Kobori, MD, PhD

- Norepinephrine and TBI-associated Prefrontal Dysfunction
  This study investigates the roles of norepinephrine signaling in the prefrontal cortex on the working memory deficit following traumatic brain injury.
  Funded by NIH/NINDS
- Dysregulation of Camp-PKA Cascade in the Prefrontal Cortex as Cause of Working Memory Deficits Following Traumatic Brain Injury
  This study is designed to investigate the temporal changes in dopamine signaling (TH phosphorylation, TH activity, dopamine release, and dopamine receptor levels) following traumatic brain injury in rodents. It will examine if manipulations designed to decrease dopamine synthesis (including GDNF application) in the hyper-excitatory phase can improve working memory performance. An understanding of the mechanisms by which brain injury alters dopamine signaling is critical for the development of mechanism-based pharmacological treatments for working memory deficits.
  Funded by TIRR Foundation

Meredith Moore, PhD

- The research interests of the Kim-Moore Lab are focused on the inheritability of neurovascular disease. Traditionally, genetic research has concentrated on disease causing single mutations in individual genes, but in recent years, this approach has expanded to include the influence of DNA structure. This field is known as epigenetics, which literally translates to "on top of genes". Epigenetic mechanisms include methylation, histone modification and the growing role of small, non-coding RNAs in regulating gene expression and cellular functions. We are examining these processes in models of traumatic brain injury, aneurysm and stroke to understand disease progression and develop novel therapeutics.

Hariyadarshi Pannu, PhD

- SCCOR in Thoracic Aortic Aneurysms and Dissections: Dysregulation of TGF-β Signaling in Thoracic Aortic Aneurysms and Dissections
  This is a Specialized Centers Of Clinically Oriented Research (SCCOR) grant project addressing the TGF-β driven mechanism of aneurysm formation. The Pannu lab focuses on identifying the molecular mechanisms that lead to vascular diseases, with the ultimate goal of using this information to improve diagnosis and therapy for cerebrovascular disease.
  Funded by NIH (Dr. Pannu is co-investigator)

Teresa Santiago-Sims, PhD

- Identification of Coding Variants Associated with Cerebral Aneurysm Pathogenesis
  The long-term goal of this project is to identify gene defects that may contribute to the development of cerebral aneurysms, to understand the pathogenesis of cerebral aneurysms at the molecular level, and to increase the ability to identify individuals at risk. The study aims to identify families affected by cerebral aneurysms and families affected by both cerebral aneurysms and aortic

aneurysms; to perform genetic linkage analyses in cerebral aneurysm families; and to identify genetic mutations involving the coding regions. Another aim is to characterize the association between identified TGFB (transforming growth factor beta, a growth factor synthesized by skeletal cells) receptor variants and cerebral aneurysm patients.
Funded by American Stroke Association-Burgher Foundation Centers for Stroke Prevention Research (Collaboration with Harvard-Burgher Center)

Nitin Tandon, MD

- Comparative Analysis of Structural and Functional Characteristics of Essential Brain Regions as Measured by Functional Imaging and Electrophysiology.
  The surgical removal of tumors or epileptic foci located close to essential regions of the brain involved in movement or language is contingent upon localizing and preserving eloquent brain regions. This study will compare the current standard for such localization--the controlled application of electrical currents--with localization utilizing functional MRI (fMRI) to detect activation of brain regions during the performance of various language and cognitive tasks. Diffusion tensor imaging, a specific type of MRI, will be used to determine how the language areas connect with each other, and to lateralize the language hemisphere likely supporting language function. The study will generate and compare maps of language function obtained using fMRI with those obtained by electrical stimulation of the brain. Additionally, in patients undergoing the chronic implantation of subdural electrodes for the localization of seizure onset sites, electrophysiology data collected during various cognitive processes will allow for interpretation of the hemo-dynamic signal used in fMRI. This multi-modal approach will address fundamental questions about the substrates, pathways and processes involved in language comprehension and production.
  Funded by UT Center for Clinical and Translational Sciences and by the Vivian Smith Foundation

Alex Valadka, MD

- Mission Connect Mild Traumatic Brain Injury Extramural Multidisciplinary Research Consortium Award
  Dr. Valadka is the Principal Investigator for the Mission Connect Mild Traumatic Brain Injury Translational Research Consortium. The long-term goal of the consortium is to improve the diagnosis and treatment of mild traumatic brain injury through collaborative basic and clinical research. The consortium includes research teams from The University of Texas Health Science Center at Houston, The University of Texas Medical Branch at Galveston, Baylor College of Medicine, Rice University, and the Transitional Learning Center in Galveston. Specific aims include 1) standardizing animal models utilizing clinically relevant neurobehavioral endpoints, 2) improving diagnosis by developing more objective criteria for early post-injury and chronic conditions, and 3) developing new and innovative treatment strategies with provision for pre-clinical and phase 1 and 2 testing of promising

treatments.
Funded by Department of Defense, Post-Traumatic Stress Disorder and Traumatic Brain Injury Research Program of the Office of Congressionally Directed Medical Research Programs

Rong Yu, PhD

- Regulation of Nrf2-Mediated Gene Expression
  Oxidative stress plays a central role in the pathogenesis of many human diseases, such as neuron degenerative diseases and cancers, and is also a contributing factor to the secondary brain cell death after primary brain injury. The purpose of this study is to explore a natural defense mechanism against oxidative stress, in particular, the role of Nrf2, a protein that controls induction of a group of antioxidant and detoxification enzymes. A long-term goal of this study is to develop effective and mechanism-based therapeutic strategies for prevention and treatment of oxidative stress-related human diseases.
  Funded by NIH/National Institute on Aging