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– Selected Recent Publications from the Department of Neurological Surgery –

Ames CP, Crawford NR, Chamberlain RH, Deshmukh V, Sadikovic B, Sonntag VK. Biomechanical analysis of a resorbable anterior cervical graft containment plate. **Spine** 2005;30(9):1031-8.

Baraban SC, Taylor MR, Castro PA, Baier H. Pentylenetetrazole induced changes in zebrafish behavior, neural activity and c-fos expression. **Neuroscience** 2005;131(3):759-68.

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Haas-Kogan DA, Prados MD, Tihan T, Eberhard DA, Jelluma N, Arvold ND, Baumber R, Lamborn KR, Kapadia A, Malec M, Berger MS, Stokoe D. Epidermal growth factor receptor, protein kinase B/Akt, and glioma response to erlotinib. **J Natl Cancer Inst** 2005;97(12):880-7.

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Ozawa T, Hu JL, Hu LJ, Kong EL, Bollen AW, Lamborn KR, Deen DF. Functionality of hypoxia-induced BAX expression in a human glioblastoma xenograft model. **Cancer Gene Ther** 2005;12(5):449-55.

Parney IF, Kunwar S, McDermott M, Berger M, Prados M, Cha S, Croteau D, Puri RK, Chang SM. Neuroradiographic changes following convection-enhanced delivery of the recombinant cytotoxin interleukin 13-PE38QQR for recurrent malignant glioma. **J Neurosurg** 2005;102(2):267-75.

Parsa AT, Wachhorst S, Lamborn KR, Prados MD, McDermott MW, Berger MS, Chang SM. Prognostic significance of intracranial dissemination of glioblastoma multiforme in adults. **J Neurosurg** 2005;102(4):622-8.

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Turner RS, Anderson ME. Context-dependent modulation of movement-related discharge in the primate globus pallidus. **J Neurosci** 2005;25(11):2965-76.

Wrensch M, Weinberg A, Wiencke J, Miike R, Sison J, Wiemels J, Barger G, DeLorenze G, Aldape K, Kelsey K. History of chickenpox and shingles and prevalence of antibodies to varicella-zoster virus and three other herpesviruses among adults with glioma and controls. **Am J Epidemiol** 2005;161(10):929-38.

BRAIN ACTIVITY

ACADEMIC AND RESEARCH NEWS VOLUME 7 NUMBER 2

IN THIS ISSUE . . .

. . . we explore the exciting research being performed by members of the Brain and Spinal Injury Center — clinicians and bench scientists dedicated to improving outcomes for patients with traumatic brain or spine injury.

CONTENTS

Neurotrauma Research at the University of California, San Francisco Gets Back to BASICs

Brain and spinal cord injury affect close to two million people in the United States each year, causing permanent functional disabilities including paraplegia and quadriplegia. To better understand the mechanisms underlying neurological injury, neurotrauma surgeons and researchers at the University of California, San Francisco have formed the Brain and Spinal Injury Center (BASIC) — a joint collaboration between the departments of Neurological Surgery and Neurology. Both departments bring their particular areas of expertise to a multidisciplinary effort centered on translational research.

"There seem to be more scientists than clinicians studying trauma, so the connection is often lacking," says **Linda Noble-Haeusslein PhD**, Co-Director of BASIC. "The feeling from scientists in the field is that it is difficult to bridge the gap between the lab and what is needed in the clinical setting." The members of BASIC are in a unique position to bridge that gap. Their location at San Francisco General Hospital, a major Level I trauma center in northern California, enables them to see and treat a broad range of injuries. The element of a strong clinical branch, which is often lacking at other trauma research institutions, allows bench scientists to work directly on the problems encountered daily by clinicians. Investigators are achieving this by incorporating what they know about human central nervous system injury into complex, clinically relevant animal models.

Geoffrey Manley MD, PhD, Co-Director of BASIC, uses a swine model to measure uptake and use of oxygen by brain tissue in order to better understand the metabolic consequences of hemorrhagic shock and the effects of resuscitation and alterations in ventilation. A large animal such as the swine is needed to realistically translate advances made in the laboratory into therapies for patients, and many medical devices first tested in swine are now used to treat humans in the ICU. "The clinical reality often refines the basic science question," says Manley. "It is a continuum, and the transition is the most exciting part."

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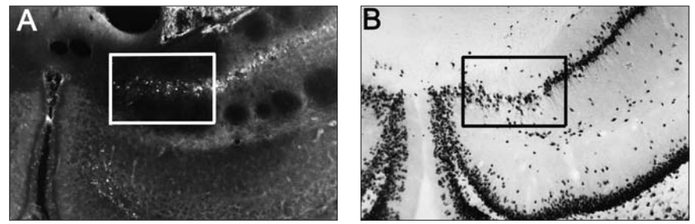


Neuronal loss is not limited to the site of cortical impact after traumatic brain injury, but rather also involves distinct subcortical regions including the hippocampus, as shown by staining of tissue sections for Fluorojade (A), a marker of cell injury, and NeuN (B), a neuronal marker. This hippocampal damage likely contributes to cognitive deficits.

LOOKING TO THE FUTURE

In the past several years, the viability of the neurotrauma care system in the United States has been threatened by financial instability, lack of public awareness, and declining numbers of neurotrauma specialists. Insufficient resources have especially impacted Level I trauma centers, which provide 24-hour availability of neurosurgeons, anesthesiologists, and orthopedic surgeons, as well as training for future trauma specialists. The closing of these centers can often be abrupt and place a large burden on surrounding hospitals. In California, Level 1 trauma centers can be as scarce as one per county, potentially requiring trauma patients to travel long distances to receive the specialized care they need.

Through a partnership with the City and County of San Francisco, the Department of Neurological Surgery has established a world-class facility at San Francisco General Hospital (SFGH), one of the major Level 1 trauma centers in northern California. Our neurosurgeons at SFGH treat hundreds of adults and children with traumatic brain and spinal cord injuries each year. In 2001, to broaden the collaboration between bench scientists and clinicians working in the field of neurotrauma research, the Department established the Brain and Spinal Injury Center (BASIC), led by Co-Directors **Geoffrey Manley MD, PhD** and **Linda Noble PhD** of the Department of Neurological Surgery and J. Claude Hemphill MD of the Department of Neurology.

The unpredictable and sporadic nature of neurotrauma has traditionally made it a difficult area of investigation. Most trauma centers do not receive enough patients to conduct conclusive studies on outcome and the mechanisms of neural injury. The BASIC group has the advantage of a large volume of patients treated at SFGH, and is using the valuable clinical data obtained there to create more relevant animal models of central nervous system injury. By using these animal models, Manley was one of the first individuals to describe aquaporin channels as an underlying mechanism for the cerebral edema associated with brain injury. Greater knowledge of the role of aquaporin channels in edema could help identify new therapeutic targets for this debilitating and often fatal condition. Manley was recently awarded an R01 grant from the National Institutes of Health (NIH) to continue work on this topic.

Grant support is vital for the future of neurotrauma research, as it is often the only source of funding powering studies in this important but often invisible field, and makes it possible to recruit and retain junior trauma neurosurgeons and nurses. The innovative and results-driven research performed by our faculty has made us the top NIH-funded neurosurgical program for the third consecutive year, and in the past year and a half the BASIC group has secured an excess of two million dollars in extramural grant support. We are also expanding the neurotrauma faculty to include two new neurosurgeons and one new basic scientist. Current national funding does not reflect the severity of the conditions that can result from neurotrauma or the subsequent cost to the community. We feel it is our responsibility, as an academic center, to make neurotrauma a central part of our research program.

Mitchel S. Berger MD
Kathleen M. Plant Distinguished Professor & Chairman

Neurotrauma Research Gets Back to BASICs

Continued from page 1

While the swine model is useful for physiological and imaging studies of brain injury, the rodent model can be used to study the basic mechanisms of both brain and spinal cord injury. One particular advantage of the rodent model is that it can mimic both primary and secondary damage. Primary damage refers to the initial mechanical damage that occurs with injury. Secondary damage (also known as autodestruction) affects the penumbral zone — the boundary between irreversibly damaged and normal tissue — causing healthy tissue to die or lose functionality following primary injury. BASIC researchers have shown that secondary damage can result from an early inflammatory response. The open communication between the parenchymal and humeral compartments that occurs when the blood-spinal cord barrier is disrupted following central nervous system (CNS) injury provides the gateway for overexuberant leukocytes to enter the CNS and break down tissue that would otherwise have remained unharmed. This process of the body unwittingly harming itself is known as inflammatory-mediated secondary tissue damage.

Adding to the complexity of the model, a cell can change its behavior depending on its location in the tissue and the time that has elapsed following initial injury. Noble-Haeusslein and her colleagues have recently used their rodent models to study the role of matrix metalloproteinases (MMP) in both the acutely and chronically injured spinal cord. They have shown that MMPs, a family of zinc- and calcium-requiring endopeptidases, play a different role in the acutely injured spinal cord than in wound healing. When the activity of MMP-9 was reduced in the acutely injured spinal cord, it resulted in stabilization of the blood-spinal cord barrier; however, the beneficial effects were lost if the MMP blockade was extended beyond the first 3 days after injury occurred, implying that the function of MMP-9 had changed. Noble-Haeusslein's goal is to develop therapeutic interventions that target these molecules' temporal windows of expression. Further investigation into how MMPs interact with the injured spinal cord will focus on their contributions to leukocyte trafficking, angiogenesis, and remodeling of the extracellular matrix.

The members of BASIC recognize the importance not only of performing this much-needed research, but also of disseminating the results to the larger neurotrauma community. With this in mind, BASIC initiated the Northern California Neurotrauma Symposium in 2002 together with the University of California, Davis. The symposium has gained in popularity over the past few years and has become an annual event. "Often researchers become so focused that we miss the overall picture," says Noble-Haeusslein. "The symposium creates the opportunity to bring the focus back to improving the clinical condition."

RESIDENT GAZETTE

Marcus Ware MD, PhD was born and raised in Indianola, Mississippi. He attended public schools and balanced his education with interests in football, tennis, and working in his family's dental laboratory. He attended college at Tougaloo College in Jackson, Mississippi where he majored in Chemistry. While in college, Ware became interested in molecular biology, and spent the nights and weekends of his sophomore year working in a laboratory at the University of Mississippi Medical Center, studying histone variants. He spent the following summers working in laboratories at the Massachusetts Institute of Technology (MIT) and the Upjohn Company.

Ware attended Harvard Medical School, where he was a student in the Harvard-MIT Health Sciences and Technology Program (HST) and the MD/PhD Program. While at Harvard, he worked in the laboratory of Christopher Walsh MD, PhD, studying molecular events in the development of the cerebral cortex. As part of his PhD thesis he identified *mdab1*, a gene required for proper cortical lamination. In addition, he also received the Harold Lamport Biomedical Research Prize for his research into the dispersion of early cortical progenitors in the ferret cortex.

Ware was graduated from Harvard in 2000 and came to the University of California, San Francisco to become a resident in the Department of Neurological Surgery. His interest turned from the development of the cerebral cortex to the genetics and treatment of brain tumors. In 2003, he received the Mahaley Award for Excellence in Clinical Research from the American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Section on Tumors for his work with **Michael McDermott MD** on surgical resection and brachytherapy for recurrent atypical and malignant meningiomas. Last year, Ware obtained a National Research Service Award from the National Institutes of Health under the mentorship of **Burt Feuerstein MD, PhD**. With this grant, he studied copy-number aberrations in gliomatosis cerebri using comparative genomic hybridization. Ware plans to pursue a career in academic neurosurgery with an emphasis on the treatment of brain tumors.

SELECTED PUBLICATIONS

Le TH, Mukherjee P, Henry RG, Berman JI, **Ware M**, Manley GT. Diffusion tensor imaging with three-dimensional fiber tractography of traumatic axonal shearing injury: an imaging correlate for the posterior callosal "disconnection" syndrome: case report. Neurosurgery 2005;56(1):189.

Auguste KI, **Ware ML**, Lawton MT. Nonsaccular aneurysms of the azygos anterior cerebral artery. Neurosurg Focus [serial on the Internet]. 2004 [cited 2005 Jul 20];17(5):[9 p.]. Available from: http://www.aans.org/education/journal/neurosurgical/nov04/17-5-13.pdf.

Ware ML, Larson DA, Sneed PK, Wara WW, McDermott MW. Surgical resection and permanent brachytherapy for recurrent atypical and malignant meningioma. Neurosurgery 2004;54(1):55-63; discussion 63-4.

Ware ML, Cha S, Gupta N, Perry VL. Radiation-induced atypical meningioma with rapid growth in a 13-year-old girl. Case report. J Neurosurg 2004;100(5 Suppl Pediatrics):488-91.

RESIDENTS' PUBLICATIONS

Acosta FL Jr, Thompson TL, Campbell S, Weinstein PR, Ames CP. Use of intraoperative isocentric C-arm 3D fluoroscopy for sextant percutaneous pedicle screw placement: case report and review of the literature. Spine J 2005;5(3):339-43.

Cha YH, **Chi JH**, Barbaro NM. Spontaneous spinal subdural hematoma associated with low-molecular-weight heparin. Case report. J Neurosurg Spine 2005;2(5):612-3.

Du R, Meeker M, Bacchetti P, Larson MD, Holland MC, Manley GT. Evaluation of the portable infrared pupillometer. Neurosurgery 2005;57(1):198-203; discussion 198-203.

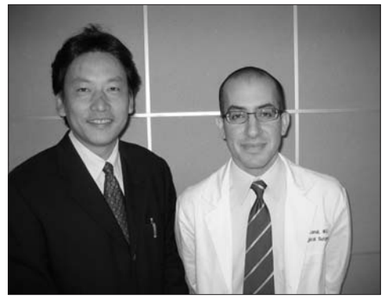
Lawton MT, **Du R**. Effect of the neurosurgeon's surgical experience on outcomes from intraoperative aneurysmal rupture. Neurosurgery 2005;57(1):9-15; discussion 9-15.

Palma V, **Lim DA**, Dahmane N, Sanchez P, Brionne TC, Herzberg CD, Gitton Y, Carleton A, Alvarez-Buylla A, Ruiz i Altaba A. Sonic hedgehog controls stem cell behavior in the postnatal and adult brain. Development 2005;132(2):335-44.

Smith JS, Quiñones-Hinojosa A, Barbaro NM, McDermott MW. Frame-based stereotactic biopsy remains an important diagnostic tool with distinct advantages over frameless stereotactic biopsy. J Neurooncol 2005;73(2):173-9.

RESIDENCY PROGRAM ADDS ROTATION AT CHILDREN'S HOSPITAL OAKLAND

The neurosurgical residency training program at the University of California, San Francisco (UCSF) is one of the largest and most prestigious in the country. One particular strength of the program is that residents are exposed to various subspecialties within neurosurgery, including pediatric neurosurgery. The UCSF pediatric neurosurgery service has been recognized for excellence in the treatment of brain tumors, spina bifida, and cerebrovascular diseases. In July 2005, a pediatric neurosurgery rotation at Children's Hospital and Research Center at Oakland (CHO) was added to the residency program. CHO is an independent, 205-bed children's hospital that provides a unique training environment for pediatrics residents and subspecialists. It is Northern California's only pediatric trauma center and possesses the region's largest pediatric intensive care unit. The Division of Neurosurgery at CHO provides a full range of inpatient and outpatient services for infants, children, and adolescents with neurological disorders and has a close working relationship with the Department of Neurological Surgery at UCSF. The director of the new rotation is Peter Sun MD, who is Chief of the clinical neurosurgery service at CHO and a member of the clinical faculty at UCSF.



Left: Peter Sun MD, Chief of the clinical neurosurgery service at Children's Hospital and Research Center at Oakland (CHO); Right: Nader Sanai MD, the first resident from the Department of Neurological Surgery to participate in the new pediatric neurosurgery rotation at CHO.

The addition of a rotation at CHO will expand the opportunities available for residents in the program. It will allow residents to gain from the unique strengths and advantages of the clinical service at CHO, including an active pediatric trauma service, a large craniosynostosis and craniofacial surgery program, and an expanding program in the management of spasticity and other functional disorders. Future plans for collaboration include the development of joint research programs that will build on the strengths of each institution.

Continued from page 3

DR. MANLEY'S SELECTED PUBLICATIONS

Claude Hemphill J, Barton CW, Morabito D, **Manley GT.** Influence of data resolution and interpolation method on assessment of secondary brain insults in neurocritical care. Physiol Meas 2005;26(4):373-86.

Manley GT, Binder DK, Papadopoulos MC, Verkman AS. New insights into water transport and edema in the central nervous system from phenotype analysis of aquaporin-4 null mice [Review]. Neuroscience 2004;129(4):983-91.

Oshio K, Binder DK, Liang Y, Bollen A, Feuerstein B, Berger MS, **Manley GT.** Expression of the aquaporin-1 water channel in human glial tumors. Neurosurgery 2005;56(2):375-81; discussion 375-81.

Oshio K, Watanabe H, Song Y, Verkman AS, **Manley GT.** Reduced cerebrospinal fluid production and intracranial pressure in mice lacking choroid plexus water channel Aquaporin-1. FASEB J 2005;19(1):76-8.

DR. NOBLE-HAEUSSLEIN'S SELECTED PUBLICATIONS

Chang EF, Claus CP, Vreman HJ, Wong RJ, **Noble-Haeusslein LJ**. Heme regulation in traumatic brain injury: relevance to the adult and developing brain. J Cereb Blood Flow Metab 2005;25:[Epub ahead of print].

Chang EF, Wong RJ, Vreman HJ, Igarashi T, Galo E, Sharp FR, Stevenson DK, **Noble-Haeusslein LJ.** Heme oxygenase-2 protects against lipid peroxidation-mediated cell loss and impaired motor recovery after traumatic brain injury. J Neurosci 2003; 23(9):3689-96.

Noble LJ, Donovan F, Igarashi T, Goussev S, Werb Z. Matrix metalloproteinases limit functional recovery after spinal cord injury by modulation of early vascular events. J Neurosci 2002;22(17):7526-35.

Yamauchi T, Lin Y, Sharp FR, **Noble-Haeusslein LJ.** Hemin induces heme oxygenase-1 in spinal cord vasculature and attenuates barrier disruption and neutrophil infiltration in the injured murine spinal cord. J Neurotrauma 2004;21(8):1017-30.

MEMBERS OF THE BRAIN AND SPINAL INJURY CENTER

Geoffrey Manley MD, PhD – Co-Director
Linda Noble-Haeusslein PhD – Co-Director
J. Claude Hemphill III MD, MAS – Co-Director (Neurology)

Chris Ames MD
Donna Ferriero MD
John Fike PhD
Grant Gauger MD
Jialing Liu PhD
Ken Monson PhD
S. Scott Panter PhD
Lawrence Pitts MD
Marco Sorani PhD
Philip Weinstein MD

In this issue, we feature part two of the Nursing Spotlight. Like the faculty, the nurses of the Department of Neurological Surgery have unique subspecialties, interests, and backgrounds. They have all developed specialized practices within the field of neurosurgery nursing, enabling them to provide expert care for patients who come to the University of California, San Francisco (UCSF).

Inna Belyaev RN was born in Russia and received her nursing degree in Odessa in 1972, with honors. After graduation, she worked as a nurse in the Odessa city hospital, first in orthopedics and neurological surgery, and then as the head nurse of the visiting nurse department, before emigrating to the United States with her family in 1979. Belyaev quickly learned English, passed her LVN exam in 1981, and passed her RN exam in 1983. She currently works as a clinical nurse in the UCSF Spine Center, assisting patients after they undergo complex spinal procedures such as artificial disk placement and spinal fusion. The position combines all of her favorite aspects of nursing: direct contact with patients, consultation, troubleshooting, symptom and pain management, and especially teaching. Belyaev has been an invited speaker at the Annual Meeting of the National Association of Orthopedic Nurses and Academy of Orthopedic Surgeons, and has been nominated for the Milton and Helen Pearl Award for Outstanding Service and the UCSF Recognition Award for Excellence in Nursing.

Michele Meeker RN began her career in Philadelphia, working primarily with patients in the intensive care unit. She received her BSN from San Francisco State University in 1990, after which she worked for eight years in the trauma and surgical intensive care unit at San Francisco General Hospital (SFGH). During that time she developed an interest in the treatment of traumatic brain injury, and in 1999 began working for the UCSF Department of Neurological Surgery at SFGH. Since then, she has worked closely with Geoffrey Manley MD, PhD and his colleagues at SFGH on clinical trials focused on improving treatment for patients who have suffered a traumatic brain injury. Meeker has also played a substantial role in the design and coordination of a large prospective longitudinal clinical trial for patients with mild to moderate traumatic brain injury, funded by the Brain Trauma Foundation. Her career achievements include launching the first waiver-of-consent treatment study in San Francisco since the new federal and state regulations mandating community consent were implemented. She is very proud to work with the dedicated group of doctors, nurses, and researchers at SFGH.

Caroline Pearson RN, MS, CPNP received her BSN in 1991 from the University of Pennsylvania. After working for a year at Children's Hospital Los Angeles, she moved to San Francisco and was hired as a staff nurse at UCSF. She worked in the pediatric medical and surgical units for five years before receiving her master's degree at UCSF in 1998. She joined the neurological surgery staff as a Pediatric Nurse Practitioner in 2000, and currently works in both the inpatient and outpatient settings. She enjoys working in a complex, acute-care environment, and is especially interested in pediatric neurology and oncology. She is proud of the collaborative approach that the Department brings to the care of pediatric patients, and is directly involved with the Department's multidisciplinary spina bifida and spasticity programs. Her other areas of interest include pediatric pain management, complementary medicine, and the multicultural aspects of healthcare.

Mariann Ward RN, MS, NP received her BSN from the University of San Francisco in 1984, graduating with honors. In 1989 she became the Seizure Surgery Nurse Coordinator for the Northern California Comprehensive Epilepsy Center at UCSF while pursuing a master's in science degree and Nurse Practitioner Certification at the UCSF School of Nursing. Since 1991 she has held a dual role as Adult Nurse Practitioner and Clinical Nurse Specialist in the functional neurosurgery service. Ward's primary areas of clinical and research interest are epilepsy and trigeminal neuralgia. She is presently the Nurse Coordinator for a National Institutes of Health-sponsored multicenter trial of Gamma Knife® radiosurgery for the treatment of temporal lobe epilepsy. In addition, her clinical practice includes a large cohort of patients with trigeminal neuralgia who are being tracked to compare and evaluate the efficacy of surgical treatments for trigeminal neuralgia, including microvascular decompression, Gamma Knife radiosurgery, and radiofrequency lesioning. In 2003, she was appointed Associate Clinical Professor in the Department of Physiological Nursing at the UCSF School of Nursing, and she enjoys teaching patients and their families as well as students, nurses, and residents.

NEUROSURGERY NOTES

For the third straight year, the Department of Neurological Surgery at University of California, San Francisco has ranked first in extramural funding awarded by the NIH to neurological surgery departments throughout the United States.

Christopher Ames MD, Assistant Professor of Neurological Surgery, has been appointed Co-Director of the Neurospinal Disorders Program in the Department of Neurological Surgery and Co-Director of the UCSF Spine Center. Ames has also performed the first L5-S1 percutaneous fusion in California, using the AxiaLTF™ system. The system uses an advanced minimally-invasive technique to access the L5-S1 vertebral bodies of the spine and enable lumbar fusion. For more information on the procedure visit www. Trans1inc.com.

Mitchel Berger MD, Kathleen M. Plant Distinguished Professor and Chairman of the Department of Neurological Surgery, has been invited to be the Scientific Program Chair of the 2006 American Association of Neurological Surgeons meeting.

Susan Chang MD, Professor and Lai Wan Kan Endowed Chair of Neurological Surgery, has been appointed director of the new Division of Neuro-Oncology. **Michael Prados MD**, Professor and Charles B. Wilson MD Endowed Chair of Neurological Surgery, has been appointed Director of Translational Research in Neuro-Oncology, to facilitate interactions between the clinical and laboratory branches of the neuro-oncology program at UCSF.

John Chi MD, MPH, resident in the Department of Neurological Surgery, received First Place at the American College of Surgeons Committee on Trauma Region IX meeting for his paper, Prehospital Hypoxia Affects Outcome in Patients with Traumatic Brain Injury: a Prospective Multicenter Study. Chi has also received a National Institutes of Health (NIH) National Research Service Award (NRSA) fellowship for his project, Polysomal RNA Antitumor Immunity.

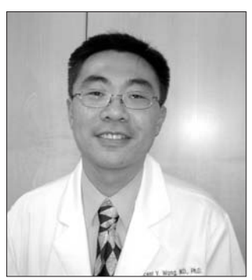
Rene Sanchez-Mejia MD, resident in the Department of Neurological Surgery, has been awarded the Ronald Tasker Young Investigator Award for his clinical research on multimodality treatment for recurrent or refractory trigeminal neuralgia. This is a national award presented by the American Association of Neurological Surgeons (AANS)/ Congress of Neurological Surgeons (CNS) Joint Section on Pain. He will present his work at the annual meeting of the CNS in Boston in October of 2005.

Justin Smith MD, PhD, resident in the Department of Neurological Surgery, has received an NIH NRSA fellowship for his project, Gene Methylation in Glioma and Normal Glial Cells: a Genome-Wide Study Using a Novel Methylation Array Analysis.

The Department of Neurological Surgery will be hosting the International Brain Tumor Symposium meeting in April of 2006. The Symposium was initiated over 30 years ago by UCSF and is attended by prestigious clinicians and researchers from all over the world.

The Department welcomes three new residents into the Neurosurgery Service at UCSF. **Edward Chang MD**, **Vincent Wang MD, PhD**, and **Issac Yang MD** have completed their Internships in the Department of Surgery, and will spend their first year as neurosurgery residents assisting the faculty on the adult Neurosurgery Service at the Parnassus Campus.

Edward Chang MD



Vncent Wang MD, PhD

Issac Yang MD

FOCUS ON FACULTY

IMPROVING OUTCOMES FOR PATIENTS WITH TRAUMATIC NEUROLOGICAL INJURY

Geoffrey Manley MD, PhD is an Associate Professor of Neurological Surgery at the University of California, San Francisco (UCSF), Chief of Neurotrauma at San Francisco General Hospital, and Co-Director of the Brain and Spinal Injury Center (BASIC). As a graduate of the Medical Scientist Training Program at Cornell University Medical College, Manley holds a medical degree and a doctoral degree in molecular neuroscience. He is an accomplished investigator whose work spans basic, translational, and clinical research. His research interests range from understanding the molecular causes of brain and spinal cord injury to improving clinical care for neurotrauma patients. He has recently defined a new molecular mechanism underlying cerebral edema that may lead to new treatments for this devastating consequence of brain injury. He is also considered an expert in the rapidly growing field of advanced neuromonitoring. His work has been presented at numerous national and international meetings. He has been awarded the General Motors Trauma Research Award and the Synthes Head Injury Research Award. He is a member of the Executive Committee of the Joint Section on Trauma and Critical Care of the American Association of Neurological Surgeons and Congress of Neurological Surgeons, and serves as Co-Director of their Neurotrauma practical course. He is also a consultant for the Prehospital Guidelines Committee for the World Health Organization.

All of Manley's research has direct clinical relevance. Cerebral ischemia resulting in secondary brain damage is one of the major factors influencing outcome after severe brain injury. The ability to detect ischemia and intervene to protect the brain against its effects may result in reduced morbidity and mortality after trauma. The goal of Manley's research in this clinical area is to determine if direct monitoring of brain tissue oxygenation and ischemic metabolites can better detect episodes of cerebral ischemia in patients with brain injury than current clinical monitoring techniques. Manley is also investigating brain oxygenation during hemorrhagic shock, metabolic monitoring of severely injured patients during resuscitation and critical care, and the role of aquaporin water channels in cerebral water transport.

Continued on page 4

MODELING INJURY AND REPAIR IN THE CENTRAL NERVOUS SYSTEM

Linda Noble-Haeusslein PhD is a Professor of Neurological Surgery at UCSF and Co-Director of BASIC. Her studies of neurotrauma have been funded by the National Institutes of Health for over 20 years. Noble-Haeusslein's interest in trauma began when she was a physical therapist working closely with patients with spinal-cord injuries. This clinical exposure served as the impetus to attend graduate school, where her studies addressed the complex interactions between damaged blood vessels and injured cells in the traumatized spinal cord. Her current research continues to reflect these interests, focusing on the dynamic interactions between inflammation, demyelination, and wound healing in the injured spinal cord, through ongoing collaborations with Zena Werb PhD and Steven Rosen PhD (Department of Anatomy), Alpa Trivedi PhD (Department of Neurological Surgery), Kimberly Topp PhD, PT (Department of Physical Therapy and Rehabilitation Science), and William Whetstone MD (Division of Emergency Medicine).

A second line of Noble-Haeusslein's research addresses the unique vulnerability of the developing brain to traumatic injury — the leading cause of death and disability in children in the United States. Despite clear biological differences between the immature brain and the adult brain, therapies specifically tailored to children do not yet exist. Noble-Haeusslein's laboratory has developed and characterized a murine model that mimics features seen in pediatric traumatic brain injury. From this experimental model, Noble-Haeusslein and colleagues have begun to learn how the developing brain responds to injury. Her collaborative studies with Donna Ferriero MD and John Fike PhD at UCSF and Jacob Raber PhD at Oregon Health and Science University suggest that the antioxidant status of the brain is a likely determinant of recovery after injury, and in fact may influence neurogenesis and the onset of cognitive deficits.

Through the unique expertise of each of her collaborators and members of her laboratory (Catherine Price-Claus, Christine Cun, Cliff Hsu, Seong Koh, Justin Lee, Yong Lin, Nino Maida, Hovhannes Manveylan, Andrea Olivas, Mathew Potts, Rama Pullela, Breset Walker, and Tomoko Yaneyama), advances are being made to better understand how the brain and spinal cord respond to injury, the underlying mechanisms of repair, and the determinants of functional recovery. These studies serve as the foundation for developing therapies that are specifically tailored for patients with brain and spinal-cord injuries.

Continued on page 4