



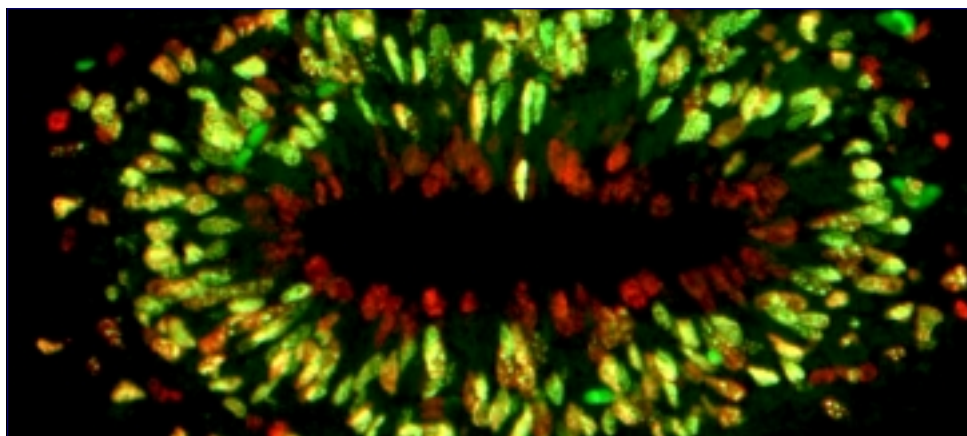
Research and development: the future of neurological surgery

by P. David Adelson, MD
Vice Chairman of Research

While much of the success individual surgeons achieve is attributed to the dedication to the art and practice of neurosurgery, many of the techniques, ideas, approaches, protocols and technical advances are attributable at some point, to a basis in the research and development in the specialty area. Each question that arises or hurdle to be surmounted with regards to patient treatment or care in the past has benefited by an investigator seeking to answer that question and improve patient outcomes.

Despite these advances there continues to be a great need for continued research efforts, particularly to elucidate the mechanisms of neurological disease and treatment. Many questions still exist, everything from basic physiology to the macro world of technologic and operative advances. The goal of the research division of the department remains and will continue to be to improve the care and treatment of patients with neurosurgical disease.

With over 30 faculty and investigators, the Department of Neurological Surgery at the University of Pittsburgh has remained at the forefront of involvement in different aspects of neurosurgical research and development. It is through this translation of research to practice that we hope to continue to define and understand the basic questions related to the cause and cure of neurosurgical disease. The two basic approaches to research and the ones that have been strengths within



Research at the Walter L. Copeland Lab: A microscopic image of a mouse brain stained using fluorescent antibodies to determine when new brain cells are generated during development and how they contribute to the newly forming brain. The orange/red cells are generated by cell division on day 15 of embryonic development; all yellow/green cells are generated after day 15.

the department have included both “basic science” which is laboratory based and “clinical research” through the care and interaction of patients.

The basic science research division of the department is based at the Walter L. Copeland Neurosurgical Research Laboratories (*see article on page 4*). Housed on the ninth floor of Scaife Hall, the lab encompasses upwards of 10,000 square feet of laboratory and office space and serves as the center for the research programs of the department. The research ongoing within the laboratories is quite varied and includes the disciplines of molecular biology, neurophysiology, neurochemistry, neuro-anatomy and other basic neuroscience arenas. Specific questions include research into the acute and chronic care following neurotrauma, neural recovery and plasticity, the neurobiologic and therapeutic response in neuro-oncology, movement disorders and epilepsy, cell death and radiation injury and cerebrovascular physiology and modeling.

While the Copeland Laboratories are the core basis for the basic science research within the department, other faculty members and investigators are collaboratively involved with a multitude of investigators and research centers throughout the university. These include the Safar Center for Resuscitation and

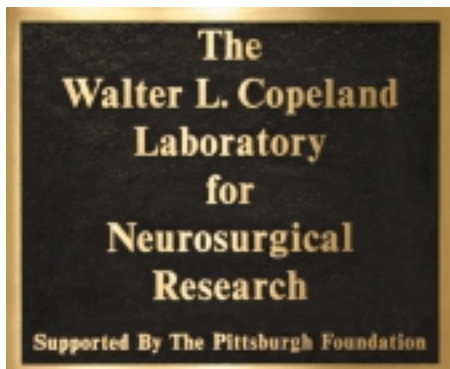
Research, the Hillman Cancer Center and many other basic and neuroscience departments throughout the university.

While the concept of “bench-to-bedside” research is a term freely utilized by many, our department carries this idea as part of its mission. Although many different areas of basic science research are integral to defining basic process, clinical neuroscience and research is necessary for changing clinical practice. Efforts by investigators are in basic science areas that will likely soon come to clinical trial in the near future. A variety of critical laboratory investigations will hopefully soon be translated into technologic and therapeutic advances and integrated into clinical trials. These types of fundamental approaches and integration into the clinical arena will continue to facilitate and improve the care of neurosurgical patients.

Clinical trials and other prospective studies and investigations continue to be a major area of research by the faculty and investigators within the department in order to improve the lives and care of patients.

Particular strengths have included clinical research in traumatic brain injury, both adult and pediatric, stereotactic and functional neurosurgery, neuro-oncology both adult and

(See *Research and development* on page 6)



The Copeland laboratories serve as the core of the department’s innovative research programs. (See story on page 4.)

Understanding and redefining the questions related to neurosurgical care.

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Robert Sclabassi, MD, PhD
William C. Welch, MD
Howard Yonas, MD
(Vice Chairman, Academic Affairs)

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C. Edward Dixon, PhD
Michael Horowitz, MD
Amin Kassam, MD
Larry W. Jenkins, PhD
Donald Krieger, PhD
Mingui Sun, PhD
John K. Vries, MD
Harold B. Weiss, MS, MPH, PhD

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Donald J. Crammond, PhD
Anthony Fabio, PhD
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Glenn Gobbel, DVM, PhD
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Daniel A. Wecht, MD

Clinical Assistant Professor

Ghassan K. Bejjani, MD

Research Professor

Edwin Nemoto, PhD

Research Assistant Professors

Ronda Pindzola, PhD
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Visiting Instructors

Ira Goldstein, MD
Thomas Steineke, MD

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Manabu Hatano, MD
Naruo Kuwasima, MD
Juan Jose Martin, MD
Jae-Gon Moon, MD
Kotaro Nakaya, MD
Daniel Prekumar, PhD
Tsukasa Sakaida, MD
Margaret S. Wilson, PhD
Hong Qu Yan, MD, PhD
Tianbing Yang, PhD

An expanding field, but a declining workforce

Neurosurgery, a sub-specialty that provides care for patients with brain, spine, nerve root, and peripheral nerve problems, has witnessed extraordinary growth during the past decade. This is in part related to an increasing need for the evaluation and treatment of spine related disorders, the incorporation of minimally invasive surgical techniques within the general context of most neurosurgical procedures, and the increasing role of neurosurgeons in endovascular, movement disorder, chronic pain, and potentially neurodegenerative disorders.

Paradoxically, during this decade, the number of neurosurgeons practicing in the United States has fallen. The reduction in neurosurgical providers has been ascribed to a number of issues: high professional liability litigation rates in states such as Pennsylvania (with no prospect for tort reform), the frustrations of dealing with managed care and the wide variety of insurance providers (we deal with over 200); the general lack of independence in practice.

Less than 150 neurosurgical practitioners finish neurosurgical training in the U.S. each year. Considerably more limit or cease their practice. Neurosurgeons in many states have opted to restrict their practice to spine related disorders only, where the liability issues are less. In some states, fully credentialed and appropriately trained neurosurgeons have opted out of providing trauma care, restricting their credentialing privileges at various hospitals to spine problems only.

Other United States academic leaders continue to report centralization of acute and traumatic neurosurgical care at tertiary or quaternary hospitals. Regional neurosurgeons, fearing the machinations of trial lawyers, have continued to refer subarachnoid hemorrhage, moderate trauma cases, and all acutely ill patients to regional centers. In the recent five years, our

department has seen the total neurosurgical case experience increased by almost 200%. We estimate that the total number of neurosurgical providers in Western Pennsylvania decreased from 51 in 1993 to 38 in 2003.

It is extremely difficult to recruit neurosurgeons to Western Pennsylvania in the present legal climate. Waffling by the governor and the state legislature, adverse rulings by the Pennsylvania Supreme Court—they ruled that malpractice tort reform requires a constitutional amendment (a three year process at best)—means that reform can only be achieved by legislation at the federal level. Regional annual malpractice rates range from approximately \$80,000 per year per neurosurgeon to up to \$250,000 per year per neurosurgeon. For this reason, there are no longer any neurosurgeons practicing in Wheeling, WV. This outcome will likely spread rapidly to Western Pennsylvania as well.

What can be done? Firstly, we need our patients to struggle together with us for meaningful liability tort reform. We can hope that action does not require a neurosurgical “blue flu.” Secondly, we must provide the best resources at institutions where advanced neurosurgical care will be centralized. Thirdly, we need to evaluate the current neurosurgical resident output, increasing the number of residents being trained in order to meet the emerging need. Fourthly, we need to re-design the resident curriculum to correspond with the practice goals of future neurosurgeons. For example, there could be three tracks for neurosurgical education, neurosurgery-spine (a four year curriculum leading to expertise in non-complex spine and restricted credentialing related to spine disorders only); neurosurgery-general could be a four-year

(See *Workforce* on page 6)



Brain Trauma Research Center aims to improve outcomes following severe TBI

by C. Edward Dixon, PhD

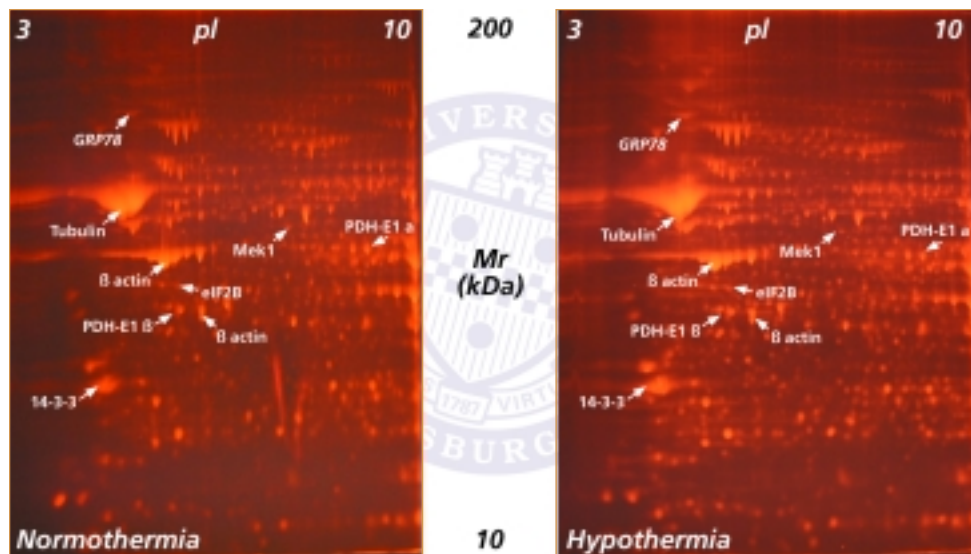
Director, Brain Trauma Research Center

The Brain Trauma Research Center (BTRC) is a multidisciplinary, multi-departmental research program aimed at improving outcome following severe traumatic brain injury.

The BTRC is anchored by a Program Project grant funded by the National Institute of Neurological Disorders and Stroke of the National Institutes of Health, NIH. The center is comprised of a core team of investigators from the Departments of Neurosurgery, Critical Care Medicine, Neurology, Nursing, and Psychiatry. The BTRC has strong links to the Safar Center for Resuscitation Research and the Department of Physical Medicine. Research conducted both at our center and at other brain injury research programs clearly demonstrates the potential for improving outcome using therapies designed to treat biochemical derangements that occur following impact to the brain. In order to identify the most critical of these sequelae of brain injury and to find newer therapies that are effective in treating them, the Brain Trauma Research Center has established several basic science brain trauma laboratories and clinical research projects.

Primary investigators include Drs. C. Edward Dixon, Patrick Kochanek, Steven Graham, Steven DeKosky, Robert Clark, and Howard Yonas. These researchers are studying the mechanisms of secondary brain injury. Specifically, they are investigating the role of inflammation, excitotoxicity, and reactive oxygen species in causing brain tissue injury following experimental blunt impact. In the clinical projects, Adult Brain Trauma clinical care and research is directed by Dr. Howard Yonas. Dr. Mary Kerr directs the BTRC Data Center and her clinical research is involved in the study of global and focal cerebral ischemia and therapeutic moderate hypothermia

Within the Department of Neurological Surgery, BTRC investigators Dr. Dixon and Jenkins are conducting basic science research aimed at minimizing secondary brain damage that occurs after the moment of impact and increasing recovery of function. Dr. Dixon's work examines the role of neurotransmitters and neurotrophic factors and their intracellular signaling



Brain trauma research in the laboratory: 2D gels stained with Sypro ruby were spot matched with existing protein databases. Selective MALDI-TOF mass spectrometry was performed on proteins known to be important in ischemic injury, such as eIF2 B, Mek, 14-3-3, and PDH proteins. The purpose of such projects shows the benefit of protein synthesis stimulating treatments after traumatic brain injury and determines the potential mechanisms of impaired protein synthesis during memory consolidation after TBI.

pathways on the induction and recovery of functional deficits after brain trauma. His lab employs neurochemical, molecular, and behavioral techniques. His team has recently found that following experimental TBI there is a delayed downregulation of dopamine transporter protein and a concurrent increase in tyrosine hydroxylase. These changes may represent a reorganization of brain to compensate for deficits in dopamine neurotransmission following brain trauma.

Dr. Dixon's lab has also shown those catecholamine agonist treatments starting one day after trauma can reduce cognitive deficits. A major objective of his lab is to discover how these various treatments produce their beneficial effects in the lab so that better treatments can be developed for clinical use. To help meet this objective, DNA microarrays are used to determine the patterns of genes are expressed in response to pharmacological therapies that enhance recovery of function after experimental TBI. The recent development of DNA microarrays has allowed scientists for the first time the ability to observe thousands of gene expression changes in parallel. The project will also determine the effects of the most effective DA agonist pharmacotherapy combined with an enriched environment on functional outcome and gene expression profiles. The results of this project will increase our knowledge of gene

expression changes associated with cognitive recovery after brain trauma.

The laboratory of Dr. Larry Jenkins focuses on the role of protein dysfunction in traumatic and ischemic brain injury using 2D gel based proteomic approaches coupled with the study of signal transduction pathways controlling protein synthesis. The purpose of one project is to show the benefit of protein synthesis stimulating treatments after TBI (hypothermia, insulin-growth factor and leucine in combination and alone) and to determine the potential mechanisms of impaired protein synthesis during memory consolidation after TBI. We are studying spatial memory and protein kinase systems modulating two key translation initiation pathways (eIF4 and mTOR) and their relationships to nutrition and trophic factor support, and the expression of brain growth involved in recovery and development after brain injury. Protein synthesis after developmental TBI is critical for normal brain growth, neuronal survival, learning and memory and synaptic plasticity. The purpose of this project is to optimize hypothermia treatments after pediatric TBI and determine if hypothermia enhances cognitive recovery by improving cold stress protein synthesis after pediatric TBI, thus providing a greater understanding of how hypothermia works and can be improved upon clinically. ■

by P. David Adelson, MD
 Vice Chairman of Research
 Director, Walter L. Copeland Laboratory

As part of the Department of Neurological Surgery's mission to improve the lives of patients through research and development, the Walter L. Copeland Laboratory suite was dedicated in November 1999 to serve as the core facility for neurosurgical basic science research. This 3,800 square foot facility, located on the ninth floor of Scaife Hall houses several research disciplines within the department including neuro-oncology, radiation biology and therapy, neurophysiology, neurotrauma and resident training. In addition, the laboratory suite provides core services in the areas of



The Walter L. Copeland Laboratory

Innovative research lab develops and tests therapies of tomorrow.

molecular biology, biochemistry, histology and immunohistochemistry. It is through the ongoing research within the Copeland laboratory that the therapies of tomorrow are being developed and tested.

Innovative research in the area of brain tumor therapies include the use of immunologic agents, the study of tumor angiogenesis, and the use of neural stem cells in order to treat brain tumors and minimize morbidity. In immunotherapy approaches to brain tumor destruction, there currently exists a trade off in terms of targeting tumor antigens without killing normal brain tissue. Possible adverse events in immunotherapy may include the induction of an auto immune response against normal brain tissue. Current research studies in the laboratory utilize dendritic cells to enhance the activity of therapeutic immunity and to prevent the destruction of normal brain tissue.

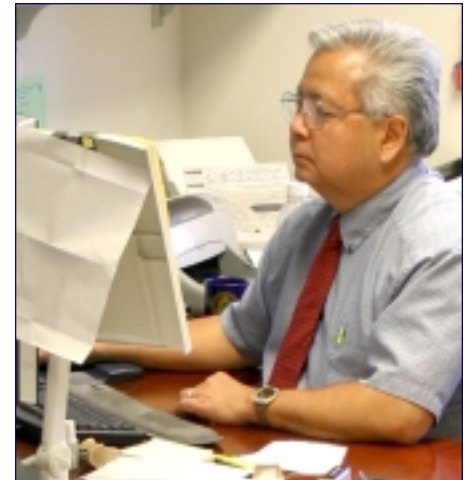
Another strategy in brain tumor research is to target the blood supply to an existing tumor so as to deprive the tumor specifically of nutrients necessary for survival. Initial studies are under way to unravel gene expression changes that occur within the microvascular endothelial cells in response to growth signals from malignant brain tumors. Potentially, interference of these signals would help to limit the growth of tumors. Through the use of Serial Analysis of Gene Expression



(SAGE), a powerful tool for analyzing gene expression changes associated with neoplasia, several genes that are selectively expressed in glioma endothelium have been identified.

Still another part of the brain tumor therapy focus is on how to improve therapy for brain tumors while minimizing damage to the surrounding normal tissue. To enhance tumor killing, genetically-engineered neural stem cells that can be transplanted into brain tumors as vehicles for the delivery of therapeutic agents have been designed and are being tested for future clinical trials.

Radiation has long been an effective method for controlling and treating cancer and in particular brain tumors. Unfortunately, radiation injury to surrounding tissue can lead to extensive and diffuse damage which can lead to neurologic morbidity. An active research program within the Copeland laboratories is looking for ways to limit or prevent damage to a normal brain as a result of radiation therapy. For reasons that are



presently unknown, the child's brain appears to be particularly sensitive to irradiation. Brain irradiation of children, used in the treatment of primary brain tumors and as a preventative measure against metastatic disease, can have severe side effects and result in significant learning disabilities. By establishing the mechanisms of radiation-induced cognitive deficits and, then developing strategies to decrease the incidence and severity of brain injury in children following radiation therapy, researchers hope to improve the potential use of radiation therapy in children with brain tumors and limit the long term impact.

The research activity of the Neurophysiology Research Group has been

particularly active with the development of biomedical sensors and electronic circuits, as well as high precision mechanical processing in support of these developments. Major developments include a 300 channel automatic EEG electrode placement system, a new skin screw EEG electrode which requires no skin preparation, and a volume conduction based implantable data communication device that transmits signals between the inside and outside of the human body. Recent work in the area of energy



metabolism and neurophysiology technology is attempting to harvest energy from the human body by converting glucose from within the body fluid into electricity in order to power implantable devices such as those implanted within the brain for the treatment of Parkinson disease and epilepsy. In this way, battery life or device failures could be minimized.

Another area of new interest has been in the area of traumatic brain injury in children. Traumatic brain injury remains the leading cause of death and disability in children affecting over 150,000 children each year. Many of these children, even those with mild concussions frequently suffer long-term

or permanent disabilities. The research group in pediatric neurotrauma at the Copeland Laboratory has focused on the acute care of children immediately following a severe injury and includes the use of hypothermia or cooling as a means to reduce secondary injury and improve outcome. Because of its history, this basic laboratory work will directly lead to a translation to clinical research. The goal of the research efforts is to not only understand the pathophysiologic response of the immature brain to injury but also to develop novel therapeutic treatments to lessen brain injury and improve long term function in these children. This model of translational research underscores the efforts in the Copeland Laboratory and future clinical trials to be directed by the department faculty.

In addition to the basic translational research within the facility, the Copeland Laboratory suite is also a central location for core services. As an essential part of resident training, Department faculty members instruct resident training courses in surgical technology and hands on techniques utilizing cadaver dissection and microvascular surgery in preparation for work in the clinical arena. Training courses are given throughout the year and are conducted in a laboratory equipped with five dissecting microscopes and a video monitoring system. The molecular biology core serves to provide expertise in molecular techniques and to facilitate the application of these protocols to neurosurgical research. Capabilities currently include gene cloning and manipulation, RT-PCR analysis of gene expression in cultured cells or tissues, *in situ* hybridization localization of mRNA expression, Western analysis of protein expression, and immunohistochemistry for protein localization. The core can also assist in bioinformatics analyses and cloning *in silico*. In addition to the molecular core, the Copeland Laboratory provides a full range of histologic services that include the preparation of histologic slides from frozen or paraffin-embedded tissue, routine staining techniques, and immunohistochemistry.

The basis of the mission of the Department of Neurological Surgery is to improve the lives and care of our neurosurgical patients. Integral to this is research into the basic science of neurosurgical disease and treatment. The Copeland Laboratories serves to provide a state-of-the-art setting where collaborative innovative research takes place. ■

Who was Walter L. Copeland?

There's an old saying that tells us that generosity and charity come from the heart. The embodiment of that spirit rests perhaps in no better place than in Walter L. Copeland, a Pittsburgh lawyer and a former director of the old Jones & Laughlin Steel Corporation. Copeland passed away in March of 1959 but his warm-hearted feelings for a 10-year-old girl he didn't know has benefited countless individuals facing cranial surgery for more than forty years.

In the late 1940's, Copeland was living with his brother, the Rev. Clyde E. M. Copeland, a pastor at the time at Jefferson United Presbyterian Church in the Pittsburgh suburb of Pleasant Hills. The pastor told his brother the story of a bright, young girl in his congregation who had developed a brain tumor. Unfortunately the child developed complications during surgery and died five months later.

Touched by the tragedy, Walter Copeland visited the child's parents at the funeral home and expressed his sympathy. A seemingly gruff individual, he never mentioned the visit to his brother, although he did later express he felt the child did not receive the best care.

Twelve years later Walter Copeland died. It was then learned that he willed over \$1.17 million for brain surgery research. No one—even Copeland's lawyers—were told the reason for this bequest, the bulk of his \$1.2 million estate.

"My brother was a very tender-hearted man and very reticent where his feelings were involved," Rev. Copeland told the *Pittsburgh Press* at the time. "He never discussed this with me, but I can only assume this (the little girl's death) is why he set up the trust fund."

Walter L. Copeland recommended in his will that income from the trust fund "be applied to further research in cranial surgery and the development of techniques in that field." He also suggested the money "be expended under the supervision of the members of the faculty of the Medical School of the University of Pittsburgh."

Through this bequest, the Walter L. Copeland Fund was established at the Pittsburgh Foundation in 1961. Since that time more than \$2.1 million has been granted to the university for various research projects. ■

Research and development

(from page 1)

pediatric, cerebrovascular and skull base neurosurgery, pain, brachial plexus and peripheral nerve disorders, and spine and spinal disorders to name but a few. Utilizing the University of Pittsburgh's leadership in such areas as neuroimaging, neurointensive care, engineering, and clinical care, patients are treated with innovative and start-of-the-art therapeutic protocols and technologies. Clinical research of these types allow for the advancement of our understanding of the human physiology response to disease and potential for treatment and cure.

New technologies, particularly in the areas of minimally invasive surgery and radiosurgery provide the potential for treatment and cure with the minimization of morbidity. In addition, our department and the university as a whole have been leaders in the area of multi-center trials which continue to be and remain the gold standard for answering clinical questions. Whether in stereotactic radiosurgery, epilepsy, or in brain trauma, randomized control trials remain the Class I data necessary for evidence based medicine to define standards of care.

Our involvement in research and development will not only continue to provide the answers to the questions that remain in neurosurgical treatment and care but also define the questions that need to be answered in the future. This rich environment will continue to move the field forward and improve the care of the patient. ■

Workplace

(from page 2)

curriculum designed to provide educational background in routine trauma management, simple spine, and common peripheral nerve disorders. Finally, for the super specialist neurosurgeon, our current seven-year curriculum would include four years of general neurosurgery and three additional years with a sub-specialty focus, for example, in complex spine, endovascular, image-guided, cerebrovascular, pediatrics, etc.

We will need to rely on the fundamental assistance of those whom we serve, our patients. They need to continue to be regarded as patients, not consumers or customers. ■

L. Dade Lunsford, MD

Chairman, Department of Neurological Surgery



Dr. Okada research team (L-R): Junichi Eguchi, MD, Tsukasa Sakaida, MD, Manabu Hatano, MD, Fumihiko Nishimura, MD, Naruo Kuwashima, MD, Hideho Okada MD, PhD, Jill Dusak.

Why immunotherapy for brain cancers?

by **Hideho Okada, MD, PhD**

Associate Professor of Neurological Surgery

Whenever I talk to people about our research on immunotherapy of brain cancers, one question is usually asked: "The brain is an immunologically privileged site. If you get an infection in the brain, it tends to be worse than anywhere else because there is not much immune protection. Do you still believe it?" or "How do you deal with the blood brain barrier (BBB)?"

These are legitimate questions and hold some truth about brain immunology. There is also the flip side of the coin with regard to the "privileged status" of the brain. The rodent version of multiple sclerosis (MS), one of the most common neurologic disorders in young population, is known as experimental allergic encephalitis (EAE). This disease model can easily be created by peripheral injection of animals with brain related antigens such as myelin basic protein.

These disease and disease models tell us that activated T-cells can cross the BBB and track down the antigen-expressing cells in the brain. In addition, in human paraneoplastic cerebellar degeneration, in which patients with ovarian or breast cancers suffer cerebellar symptoms such as ataxia, the essential pathogenesis has been revealed to be a specific T-cell response reacting against an antigen shared by breast and ovarian cancers and normal cerebellum.

The antigen, cdr2, is expressed in normal cerebellum, but the T-cell immune response is activated only after the antigen is exposed to the systemic immune system through its expression in cancer tissues. The resulting T-cell response can then recognize

and attack immune targets located in the central nervous system. We would like people to share the following message with us; brain-located antigens may not be seen very well by immune system, but once these brain antigens are exposed to the systemic immune system efficiently, we may be able to induce effective T-cell responses against the brain-located targets. Unlike other antigens that are distributed throughout the body, brain tumor specific antigens are unlikely to eliminate auto-reactive T-cell precursors via positive/negative selections.

To us, it seems that the brain is also privileged in a favorable way. To apply this for brain cancer treatment, we just need to know the targets for brain cancers and the most effective ways for vaccinations. This is the essence of what we believe and what we are doing, both in our basic and clinical studies.

We have been trying to establish creative and productive interface between the clinical and basic aspects of brain tumor research. We are one of the first groups to identify glioma specific cytotoxic T-cell epitopes. Our group is the only one in the nation running clinical trials of cytokine gene inserted glioma vaccines. We utilize multi-disciplinary approaches in our research including molecular genetics on novel cytokines, immuno-biology and most importantly, wonderful teamwork with our clinicians.

Our laboratories and offices are located in the new Hillman Cancer Center in the Shadyside section of Pittsburgh. For more information on our work, please contact us at (412) 623-1111. ■

Department Annual Report Receives Recognition

The 2003 Department of Neurological Surgery Annual Report received best of category recognition in the 38th Annual Exhibition of Western Pennsylvania printing awards. The awards are sponsored by the Printing Industry of Western Pennsylvania and recognize "excellence of achievement, effort and talent" for productions in the advertising, marketing and public relations fields. The publication was designed by **Paul Stanick**.

Walter L. Copeland Grants Awarded

The following research projects were awarded grants by the Pittsburgh Foundation. These projects represent state-of-the-art science initiatives that will hopefully be major scientific findings in the future. One of the Copeland Fund's missions is to fund pilot projects that are promising for potential future extramural funding such as the NIH.

- "Identification of Human Glioma Rejection Antigen-Tcell Epitopes," **Naruo Kuwashima, MD**.
- "In vivo delivery of shRNA for antiangiogenesis based brain tumor gene therapy," **Kevin Walter, MD**.
- "Neural Stem Cell Therapy for Traumatic Brain Injury: Functional Outcomes and Cell Differentiation," **Anthony Harris, MD, PhD**.
- "Human Bone Marrow-Derived Novel Cellular Vehicle for Brain Tumor Gene Therapy," **Tsukasa Sakaida, MD**.
- "Dopamine and DARPP-32 signaling mechanisms following traumatic brain injury in rats," **Margaret Wilson, MD**.
- "Effect of Acupuncture on Traumatic Brain Injury (TBI) in Rats," **Hong Qu Yan, MD, PhD**.
- "The effect of FiO2 elevation on local brain tissue oxygenation (PbtO2) and oxidative stress in patients with severe TBI," **Ava Puccio**.
- "Adrenergic Activation and Cerebral Ischemia After SAH," **Edwin Nemoto, PhD**.
- "Suppression of Astrocytoma Cell Invasive Migration Via Competitive Peptide Inhibition of Akt/GSK3/GS Mediated Energy Metabolism," **Marie Beckner**.
- "Dendritic Cell-Based Cytokine Gene Immunotherapy for Central Nervous System Tumors," **Hideho Okada, MD, PhD**.

Grants

- "Randomized Third-Party Blinded Multicenter Clinical Trial to Determine the Safety and Effectiveness of Oxiplex/SP Gel," **Joseph Maroon, MD**, FzioMed, Inc. (\$63,525). Clinical Trial to evaluate the safety and effectiveness of Oxiplex/SP Gel for the reduction of pain and symptoms following lumbar disc surgery.

Milestone

On November 14, 2003, the Center for Image-Guided Neurosurgery performed Gamma Knife® radiosurgery on its 6000th patient. The center performed the first Gamma Knife procedure in North America in 1987 and continues as a leader in the field, attracting patients worldwide.

Media

- **John Young Keun Lee, MD**, PGY-6 resident, was featured in a September 2003 article in the *Journal of Korean Neurosurgery*.

Promotions

- **William Welch, MD**, was promoted to full professor.
- **Harold B. Weiss, MS, MPH, PhD**, was promoted to associate professor.

Announcements

- **P. David Adelson, MD**, was elected secretary of the Congress of Neurological Surgeons.
- **Douglas Kondziolka, MD** served as visiting professor at the University of Manitoba, November 20-22.
- **Peter Gerszten, MD** served as visiting professor at Stanford University on January 8.

Welcome

Erica Batson, research specialist for Glenn Gobbel, DVM, PhD; **Audrey Bauch**, research nurse for Dr. Adelson; **Linda Hand**, research nurse Dr. Adelson; **Kelly Powell**, appointment secretary for L. Dade Lunsford, MD and Dr. Kondziolka; **Mimi Ranallo**, transcriptionist; **Dara Tomassi**, financial analyst.

Awards

- **Daniel Geynisman**, medical lab student working with Dr. Walter and Ellie Carson-Walter, PhD, has won the annual Lucien Rubinstein award from the American Brain Tumor Association. The \$1,000 national award is presented annually to the medical student submitting the best summer research project to the ABTA.

- **Emily Lehmann**, a second year University of Pittsburgh medical student, won a Certificate of Merit Award for Excellence in Biomedical Science Research from the School of Medicine dean for her summer research project regarding the CyberKnife.

- The following individuals were listed on the UPMC Health System employee recognition *Above and Beyond* honor roll: **Lois Burkhart**, Microvascular Neurosurgery clinic coordinator;

Michele Kaus, NICU nurse; **Cheryl Rodgers**, Gamma Knife® nurse; **Janet Rush**, 7G nurse; **Joyce Segal**, 7G nurse.

Congratulations

- New baby boy (Andrew Jacob, November 15) to **Melissa Lukehart**, resident coordinator, and husband Scott.

- **Grace Yum**, Gamma Knife® system programmer, adopted a baby girl (Emily).

Upcoming Events

- February 27-29: **Pittsburgh Neurotrauma and Critical Care Course**. Course covering the systemic, skeletal and soft tissue considerations in managing critical care patients for both head and spine patients. Developed for senior residents having an interest in trauma care. Contact Patricia Keeney at (610) 695-2408.

- March 8-12: **Principles and Practice of Gamma Knife Radiosurgery**. Training course targeted at neurosurgeons, radiation oncologists and medical physicists interested in Gamma Knife radiosurgery education. For more information, contact Charlene Baker at (412) 647-6250.

- March 26: **Advanced Dose Planning and Functional Radiosurgery Course**. A functional, advanced dose planning training course targeted at neurosurgeons, radiation oncologists and medical physicists working with a Gamma Knife radiosurgery unit. For more information, contact Baker at (412) 647-6250. ■



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Researchers begin carotid stenting trial testing distal protection device

The Department of Neurosurgery in conjunction with the Department of Surgery's Division of Vascular Surgery and the Department of Neurology have begun a carotid stenting research trial which compares carotid angioplasty and stenting with a distal protection device (DPD) to carotid angioplasty and stenting without the use of a DPD.

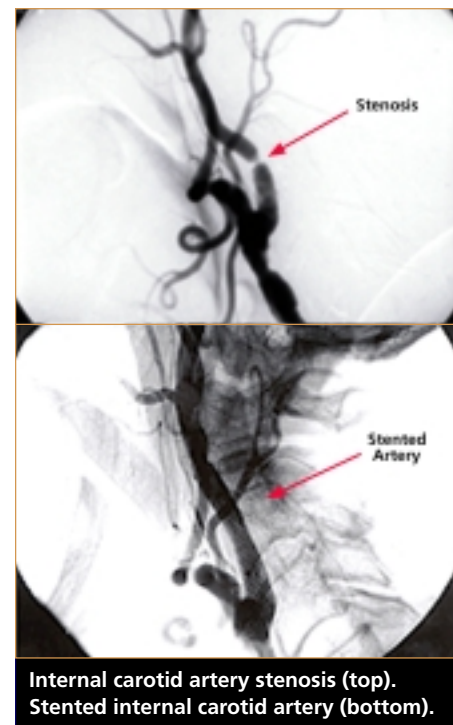
While the DPD has been incorporated into many carotid stenting protocols with the belief that it will reduce embolic events during angioplasty and stenting no randomized prospective study has ever been performed that shows true added value through the use of a DPD.

The DPD is a small wire mounted umbrella that is placed distal to the stenosis so that when the angioplasty and stenting is carried out any loose material that breaks away from the vessel wall or plaque is captured within the umbrella's net before the emboli can enter the intracranial circulation. At the

end of the procedure the net along with any captured material is closed and withdrawn from the patient.

Up to this point in time neurosurgeons at UPMC have performed all carotid stenting procedures in high risk patients who are not surgical candidates (approximately 100 cases) without a DPD and have experienced a new neurologic injury rate (temporary or permanent) of approximately 3.2%. While this rate is comparable to or better than the neurologic injury rate after open carotid endarterectomy it is felt that the use of a DPD with carotid angioplasty and stenting may reduce the rate below 1%.

The study is open to patients with a symptomatic or asymptomatic common carotid or internal carotid artery stenosis measuring > 70%. All patients must be considered a high risk for traditional open carotid endarterectomy. Specific inclusion and exclusion criteria can be found at the website address listed below. ■



Internal carotid artery stenosis (top).
Stented internal carotid artery (bottom).