



# Vaccines for brain tumors

## *a new treatment strategy*

by Claire Collins  
UPMC News Bureau

**A** new vaccine approach being studied at the University of Pittsburgh Cancer Institute (UPCI) is using multiple antigens to bring about an immune response to brain tumors, or gliomas—highly lethal, primary tumors that are difficult to treat successfully since they aggressively invade the folds and creases of the brain.

In the study, four different antigens, proteins found on the surface of tumor cells, are modified to look more dangerous, potentially soliciting a strong response by the immune system’s dendritic cells. These cells act as the quarterbacks of the immune system and coordinate the system’s attack against foreign invaders.

The project, headed by Hideho Okada, MD, PhD, assistant professor of neurological surgery at the University of Pittsburgh School of Medicine, is based on an “off the shelf” vaccine approach in which antigen peptides are synthesized and ready to use when needed. Once the peptides have been synthesized, the vaccine is introduced to glioma cells in the body.

To synthesize the antigen peptides, Dr. Okada and his team create modified peptides that are capable of activating an immune response by combining them with a class of helper peptides and dendritic cells. The dendritic cells are loaded with information about the tumors cells so that they will communicate to the T-cells to attack once the vaccine has been introduced to the body. The goal is that the modified antigen peptides will be recognized by the immune cells and elicit a strong immune response.

Given that all brain tumors are different, as are their immune responses, Dr. Okada believes a multi-antigen approach has the best potential for success. “One of the benefits to testing multiple antigens is that you will be

less likely to miss your target and more likely to get a response,” he said.

Dr. Okada adds that given the lack of effective treatments for brain tumor patients, immunotherapeutic approaches have a real potential for success because of the ability for immune cells to migrate into the central nervous system and selectively destroy malignant cells that have infiltrated tissue there.

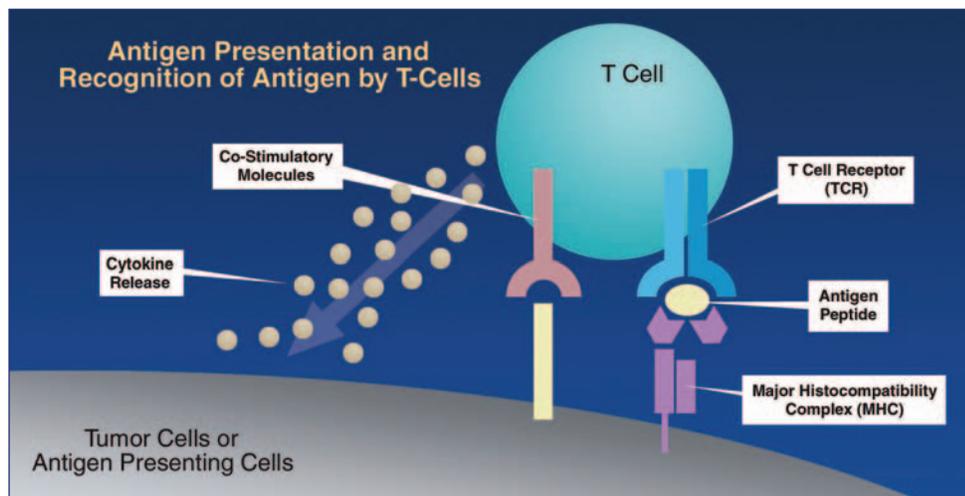
Malignant gliomas make up the majority of primary brain tumors and cause the deaths of more than 12,000 brain cancer patients each year. One of the most common gliomas, glioblastoma multiforme, has an average survival of only 12 months. Standard treatments, such as chemotherapy and radiation, are difficult to use successfully without damaging the surrounding healthy brain tissue. •

For more information on this and other brain tumor research projects underway at the University of Pittsburgh, visit the research section of our website at [www.neurosurgery.pitt.edu/research](http://www.neurosurgery.pitt.edu/research).

*“We see our approach as a more practical and potentially life-saving one.”*

Hideho Okada, MD, PhD  
Project Investigator

“We developed our vaccine based on four different tumor antigens that are commonly found in glioma tumors,” explains Dr. Okada. “This is a much more practical approach than creating vaccines from a patient’s own tumor cells because of the limited life expectancy of patients with brain tumors. By the time you have cultured a patient’s own vaccine cells, a process that can take up to six weeks, the patient’s cancer has already progressed to the point where there is nothing more we can do clinically. We see our approach as a more practical and potentially life-saving one.”



Tumor-antigen peptide bound to the major histocompatibility complex (MHC) is recognized by the T-cell receptor (TCR), which triggers the secretion of cytotoxic effector molecules, such as perforin, to exert the anti-tumor cytotoxic effects.

## Transition at the Department of Neurological Surgery

**D**uring the 2005-2006 academic year, we have had two major transitions in senior faculty. Such transitions are not unusual, but we always want to ensure that they are not engendered by professional or socioeconomic issues. Both faculty members have served as role models and mentors for many of our trainees and as valuable colleagues in the Department of Neurosurgery.

Dr. Howard Yonas, Peter J. Jannetta Professor of Neurosurgery at the University of Pittsburgh, assumed the responsibilities of chief of neurosurgery at the University of New Mexico at Albuquerque. He took with him years of accumulated experience in the management of a wide variety of neurosurgical problems, with a special emphasis on vascular disease of the brain. Howard was ready for this additional leadership challenge and moved west with a variety of plans for building and growing an academic neurosurgery program in a challenging environment.

Recently, A. Leland Albright, MD, Children's Professor of Neurological Surgery in our department, announced that he has accepted a position as professor of neurosurgery at the University of Wisconsin effective June 1, 2006. Leland has served as a member of our academic department for more than 25 years. During that time, he mentored a large number of residents and fellows. For more than ten years, he served as chief of neurological surgery at Children's Hospital of Pittsburgh. During that interval, Leland oversaw the development of one of the premiere pediatric neurosurgical experiences for our residents, and a sought after fellowship for sub-specialty training in pediatric neurosurgery. The volume of cases and the research portfolio grew dramatically, with a concentration in brain tumor management and CNS injury. Leland has served as a valuable colleague and an inspirational leader to our trainees and to our faculty. Leland provided a moral compass to me and other

members of the department as we analyze and balance issues of patient care, new directions, and innovation. During more recent years, his clinical focus centered on pediatric movement disorders, especially primary and secondary dystonia. During his years on our faculty, Leland has devoted time and energy to providing neurosurgical pediatric expertise in third world environments.

Leland and Howard will be missed by all of us. We are reminded of the three requirements for personal and professional homeostasis, as reported in the literature by our colleague, Dr. Joseph Maroon. The profession of neurosurgery is a delicate balance of personal, professional and spiritual needs. The personal needs include our families and friends. Our professional roles require us to balance patient outcomes, innovation, and to find a satisfying professional niche, especially in a large department such as ours. The spiritual needs do not encompass just our particular religious or philosophic backgrounds, but the general ethical beacons that help to guide us, to eliminate conflicts of interest, to obtain success or solace as circumstances may warrant. The balance of professional, personal and spiritual needs facilitates our enjoying a successful and satisfying life. In some cases, issues of our personal lives, many of which have played second fiddle to our goals of professional success in prior years, become critical to solve. This refocusing requires that we move on to another phase of our life, including professional relocation. Both Drs. Yonas and Albright found that new personal goals could best be achieved in another academic location. Such transitions are never easy for those individuals whom they leave behind. While we regret these transitions, we know that both Howard and Leland leave behind a feeling of a job well done, a mission accomplished, thousands of grate-

(see *Transition* on page 6)



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# Isolating, characterizing selective targets of brain tumor angiogenesis shows promise for developing therapies to delay, prevent tumor growth

by Kevin Walter, MD

Assistant Professor of Neurological Surgery

Beginning in 1971, Judah Folkman hypothesized that malignant tumors were dependent upon their blood supply in order to grow and metastasize. He popularized the phrase "tumor angiogenesis" to describe the ability of a growing tumor to develop its own, unique vascular network from the pre-existing host vessels, thereby supplying itself with nutrients and oxygen. He hypothesized that blocking angiogenesis would inhibit tumor proliferation and metastatic spread. He went on to isolate several tumor angiogenesis factors (TAFs) that were secreted by the tumor to elicit vascular growth by the host. We now know these TAFs include Vascular Endothelial Growth Factor (VEGF), Platelet Drive Growth Factor (PDGF), Basic Fibroblast Growth Factor, (b-FGF) and Scatter Factor/Hepatocyte Growth Factor (SF/HGF).

During the subsequent 35 years, additional research on the topic has led to the development of new drugs that can block angiogenesis by inhibiting TAF signaling cascades. Novel agents like Celastrol and Avastin have entered into clinical trials at the University of Pittsburgh as part of our involvement with the North American Brain Tumor Consortium (NABTC) and are beginning to show promise in the fight against brain tumors.

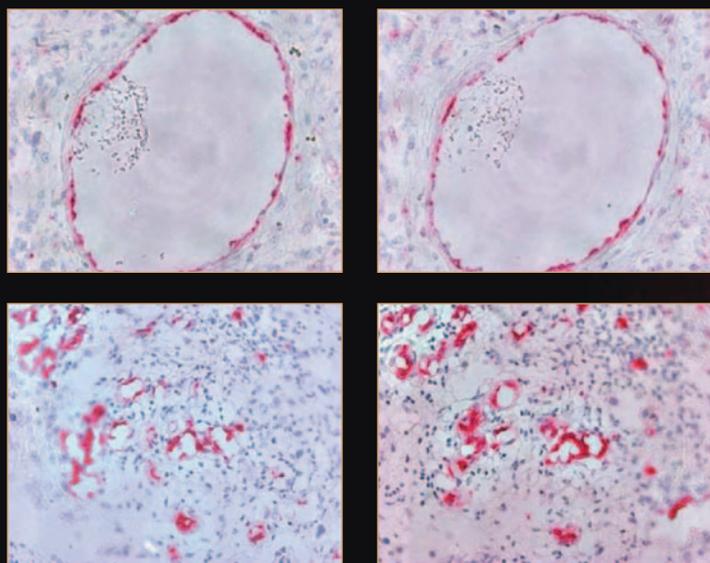
In the Copeland Laboratories, we are working to increase the number of targets that could be considered for anti-angiogenesis therapy. Most research to date on this phenomenon has focused on interrupting the signaling pathways induced by angiogenic factors secreted by the growing tumor. Less is known about the selective targets induced on the endothelial cells themselves by the circulating TAFs. Because endothelial cells represent normal tissue, they rarely mutate or become resistant to chemotherapeutic drugs. Therefore, targeting the endothelial cells rather than targeting changes in highly volatile tumor tissue has a greater chance for success. We adopted the strategy of identifying Glioma Endothelial Markers (GEMs) that are selectively expressed on growing brain tumor endothelium but which are not present

on normal endothelium. In 2004, we published the initial results of our investigation in the American Journal of Pathology. By using a gene profiling technique known as SAGE in collaboration with scientists at Genzyme Corporation, we were able to isolate 19 gene products that were significantly and selectively upregulated in brain tumor endothelium, but which were absent in normal brain endothelium. We hypothesized that inhibiting the expression of these genes would reduce brain tumor angiogenesis without harming surrounding normal brain tissue.

In collaboration with Dr. Shi-Yuan Cheng of the University of Pittsburgh Cancer Institute, we have developed animal and in vitro models of brain tumor angiogenesis to study genetic manipulations of these GEMs. One gene, known as Plasmalemmal Vesicle Associated Protein-1 (PV-1), has been particularly promising as a new target for brain tumor angiogenesis therapy. PV-1 is a molecule which is expressed in immature brain endothelium, but which disappears upon formation of the blood brain barrier. It is not expressed in the adult brain wherever the BBB is intact. Its re-emergence in the setting of brain tumors indicates that it may be a good target for selectively inhibiting proliferating brain endothelial cells.

We engineered a short RNAi duplex to knock down gene expression of PV-1 in vitro. When we inhibited PV-1 in human microvascular endothelial cells, the cells lost the ability to form tubules or vascular networks. Additionally, when we examined a large panel of brain tumors taken from a variety of patients we

(see *Brain Tumor* on page 6)



(Above) *In situ* hybridization for endothelial specific markers PV-1 (left column) and VWF (right column) in glioblastoma. (Right) Immunofluorescence staining of a microcapillary immunomagnetically isolated from a patient with malignant glioma.

# Neurooncology program sets sites on novel treatments for brain tumor

by Frank Lieberman, MD  
Director, Adult Neurooncology Program

The North American Brain Tumor Consortium (NABTC) is one of two multicenter clinical trials groups established by the National Cancer Institute to develop novel treatments for patients with brain tumors. Since its inception, the NABTC has focused on translating molecular biologic discoveries regarding brain tumors into clinical trials, and the UPMC Neurooncology Program has been an active member since the inception of the NABTC.

Currently the consortium's clinical trial program focuses on evaluating molecularly targeted drugs for the most common type of malignant brain tumors, the malignant gliomas. These drugs have been designed to attack malignant gliomas by affecting signaling pathways that drive tumor cell growth, spread, or development of tumor blood vessel supply.

During the 1990's we performed a series of clinical trials evaluating the first generation of molecularly targeted drugs. As principal investigator for UPMC Cancer Center's participation in the NABTC, I served as national study chair for one of these studies, which examined the drug Iressa. The knowledge gained from these studies has led to the second generation of clinical trials, in which molecularly targeted drugs, which attack different molecular signaling pathways, are being combined.

The NABTC clinical trials strategy is to first evaluate new drugs or drug combinations in patients with recurrent malignant gliomas. In order to determine whether the drugs are having the predicted effect on the tumor, NABTC studies frequently recruit patients who will be undergoing surgery as part of their clinical care, so that patients will receive several doses of the experimental regimen prior to surgery.

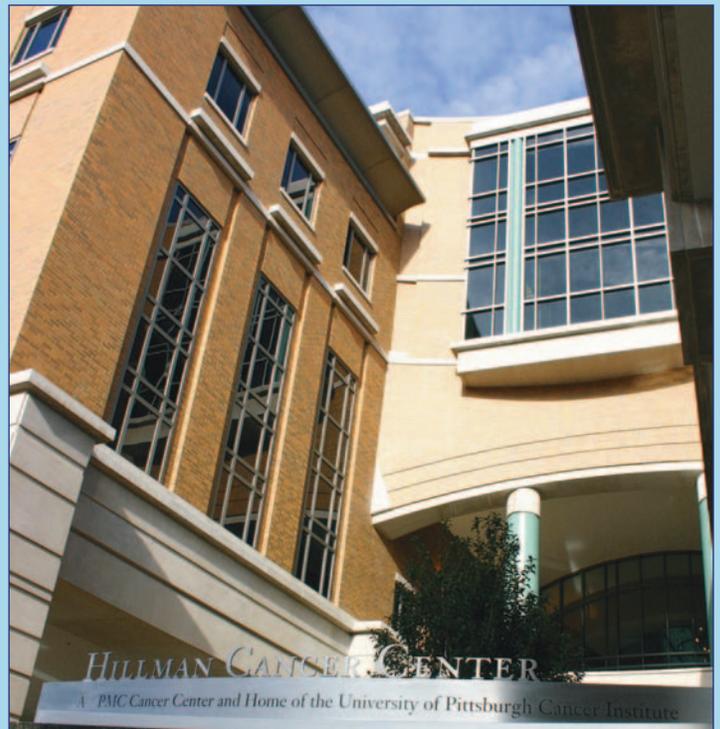
Tumor tissue that is removed during the surgery is examined in the laboratory to determine if the drugs have "hit the target" and if so, whether the expected molecular changes in the tumor that predict tumor response are occurring. This is an important step in understanding how to develop the most effective treatment strategies.

The UPMC Neurooncology Program works closely with the neurosurgeons caring for the patients to facilitate clinical trial participation for patients who need surgery for recurrent malignant gliomas. In order to give the experimental drugs the best chance of demonstrating what they can do, many of the NABTC trials for recurrent malignant gliomas accept patients with either only the first, or in some cases up to two prior recurrences.

The current repertoire of clinical trials includes drugs with a range of targets, attacking malignant gliomas in a variety of ways. These include drugs that interfere with the tumor's ability to establish and maintain a blood supply. These drugs, called antiangiogenic agents, have been effective in other solid tumors, and are now being tested extensively in NABTC trials.

The Investigational MRI Program at UPCI, headed by Dr. Erik Weiner, has developed an imaging technique called Dynamic Contrast Enhanced MRI to measure the effects of antiangiogenic drugs on the blood supply of brain tumors. This protocol is being incorporated into an upcoming NABTC trial testing the drug VEGFtrap.

NABTC trials are designed to provide as much information as possible about how the experimental treatments are working at the molecular level, in addition to the most important mission of identifying those treatments that control tumors and prolong survival. The results of molecular genetic studies of tumors from patients in recently completed trials of drugs that block signaling through the EGFR (epidermal growth factor receptor) pathway are beginning to unravel the mechanisms that



The Adult Neurooncology Program is based at the Hillman Cancer Center. Hillman is the flagship treatment and research facility of the UPMC Cancer Centers network. It serves as a home to internationally regarded surgical, medical and radiation oncology specialists, who perform treatment procedures unavailable elsewhere in the region. The center also has the region's most advanced imaging technologies to detect cancer and monitor treatment. Opened in 2002, the center was made possible, in part, through the generosity of Henry L. Hillman and the Hillman Foundations.

tumors use to escape the drugs effects. Current NABTC trials include drugs and combinations which target: EGFR, antiangiogenic drugs, histone deacetylase inhibitors, and combination studies targeting multiple pathways such as EGFR and AKT simultaneously.

Our patients play a crucial role in NABTC trial success. Patients are truly the irreplaceable pioneers in brain tumor research, and we recognize the courage and commitment of our study subjects. Although NABTC trials by their nature demand a great deal of commitment from patients we try to design the studies to be as user friendly as possible.

Current and planned clinical trials are recruiting patients with recurrent glioblastoma, newly diagnosed glioblastoma, and recurrent malignant astrocytoma. Some NABTC trials are open at UPMC Cancer Center Network sites in addition to Hillman Center, and several studies are testing oral drugs (pills) which patients can take at home. In addition, there is a phase 2 clinical trial for patients with recurrent CNS lymphoma using Rituxan and temozolomide.

The Adult Neurooncology clinical trials team includes medical neurooncologists, neurosurgeons, a neuropathologist, neuroradiologists, and most importantly, our experienced research nurse coordinator Rita Johnson, RN.

Up-to-date information about the open NABTC trials, eligibility, and how to participate in our clinical trials is available by contacting Johnson at (412) 647-8571, (800) 237-4727 or [johnsonr1@upmc.edu](mailto:johnsonr1@upmc.edu). In addition, potential patients and referring physicians can contact me at (412) 692-4724 or [liebermanf@upmc.edu](mailto:liebermanf@upmc.edu).

Extensive information about the University of Pittsburgh Cancer Institute and the Hillman Cancer Center can be found at [www.upci.upmc.edu](http://www.upci.upmc.edu). This site describes the academic, educational and institutional environment of the cancer center.

# Pediatric brain tumor studies focus on improving prognosis, quality of life

by Ian Pollack, MD

Walter Dandy Professor of Neurosurgery  
Chief, Pediatric Neurosurgery  
Children's Hospital of Pittsburgh

(Editor's Note: Dr. Pollack is also director of the Brain Tumor Program at the University of Pittsburgh Cancer Institute.)

**B**rain tumors are the most common solid tumors of childhood and have the highest mortality rate. Because there are diverse subtypes of brain tumors, which require histology and age-specific treatment approaches, therapeutic studies are commonly coordinated by multi-institutional consortia, such as the NIH-supported Children's Oncology Group (COG) and Pediatric Brain Tumor Consortium (PBTC), the latter an investigational study group examining novel agents and therapeutic strategies for children with brain tumors.

The University of Pittsburgh and Children's Hospital of Pittsburgh are one of a handful of institutions that belong to both groups, as well as to one of the NIH-supported adult consortia, which affords patients with a broad range of treatment options.

During the last 10 years, the COG and its predecessors, the Children's Cancer Group and the Pediatric Oncology Group, have made a number of observations that are influencing current treatment approaches:

1) Such studies have demonstrated strong associations between extent of tumor resection and outcome for ependymoma, low-grade glioma, high-grade glioma, and medulloblastoma, an improvement issue in the neurosurgical care of children with these tumors.

2) Use of adjuvant chemotherapy has allowed reduction in craniospinal radiotherapy doses to 2340 cGy from 3600 cGy in children with extensively resected non-metastatic medulloblastoma, with greater than 75% 5-year survival.

3) Moderately intensive adjuvant chemotherapy has been observed to improve survival in metastatic medulloblastoma.

4) The feasibility of radiotherapy dose reduction in conjunction with pre-irradiation chemotherapy has been demonstrated for germinoma.

5) Intensive induction chemotherapy has been shown to have activity for infant brain tumors, although the observation that long-term disease control is suboptimal has prompted additional therapeutic modifications, which incorporate molecular data in treatment stratification.

6) Molecular factors that correlate with outcome of PNETs and high-grade gliomas have been identified, the latter studies conducted in large part at the University of Pittsburgh, and are being assessed in prospective studies.

Notwithstanding improvements made for certain tumor types, others such as diffuse brainstem gliomas, continue to carry a dismal prognosis. Accordingly, the COG and PBTC are continuing to evaluate novel agents and treatment strategies for

patients with these challenging tumors. Of particular interest from the neurosurgical perspective, is the administration of immunotoxins targeted to receptors selectively expressed on tumor cells versus normal cells, which are delivered by convection-enhanced delivery techniques. Such studies for children are being performed exclusively within PBTC institutions, such as the Children's Hospital of Pittsburgh.

It is also important to emphasize that children who survive their disease often experience sequelae from the tumor or treatment that compromises quality of life. Accordingly, ongoing studies are focusing on improving the prognosis of children with tumors resistant to prior therapies and reducing

late sequelae among children with treatment-responsive tumors, using results of previous studies as a foundation upon which to build new, and hopefully improved, treatment strategies. •



For more information on pediatric brain tumors, please visit the oncology section on the Children's Hospital of Pittsburgh website at [www.chp.edu/greystone/oncology/tumor.php](http://www.chp.edu/greystone/oncology/tumor.php).

## Brain tumor angiogenesis

(continued from page 3)

found nearly uniform upregulation of PV-1 in all forms of high grade, malignant brain tumors. We also demonstrated that PV-1 was induced by the growth factors secreted by the brain tumor and that we could elicit this response both in vitro and in vivo. We have now begun to extend our evaluations of potential targets to further molecules identified in our SAGE studies. Another molecule, TEM1, appears to behave in a fashion very much analogous to PV-1. Namely, we have been able to detect it widely in aggressive brain tumors, but not at all in the quiescent non-proliferating brain endothelium. Preliminary data indicates that it may also play a critical and vital role in brain tumor angiogenesis.

It is also possible that induction of these genes may be related to altered blood brain barrier integrity associated with cerebral edema in the setting of progressive brain tumors. Not only may inhibiting the function of these genes delay tumor growth, but it may also reduce cerebral edema and morbidity associated with brain swelling in brain tumor patients. With the help of Dr. Martina Stippler, we have begun to adapt an in vitro model suitable for the study of these molecules as modulators of blood brain barrier permeability in the laboratory. We expect that by characterizing the blood brain barrier in this manner we may be able to improve therapy for cerebral edema in the setting of glioma.

We are also trying to exploit the differential regulation of brain tumor endothelial gene expression as a novel method for the early detection and diagnosis of brain tumors. The majority of the 19 gene products identified in our SAGE screens represent cell membrane or extracellular proteins that can be detected in serum. Dr. David Atteberry, in conjunction with Drs. William Bigbee and Anna Lokshin of the University of Pittsburgh Cancer Institute, have been employing proteomic based techniques including SELDI-TOF-MS and xMAP to look for characteristic angiogenesis signatures in the blood of patients with malignant glioma. •

## Department of Neurosurgery transition

(continued from page 2)

ful patients, and a legacy of trainees thankful for the opportunity to have learned from them.

Dr. Albright leaves behind three superb colleagues, Ian Pollock, MD, chief of pediatric neurosurgery, P. David Adelson MD, department vice chairman for research, and Dr. Elizabeth Tyler-Kabara, MD, PhD. Dr. Albright shares in my enthusiasm for the nomination of Dr. Adelson as the first Leland Albright Endowed Chair and Professor of Neurosurgery at the University of Pittsburgh.

As we look forward to 2006-2007 academic year, we welcome Costas Hadjipanayis, MD, PhD, who will augment our general neurosurgery and brain tumor program, David Okonkwo, MD, currently chief resident at the University of Virginia who will energize our commitment to clinical care in CNS injury, and Matt Wetzel, MD, a long-sought colleague of Michael Rutigliano, MD, in our Westmoreland County Community Neurosurgery Center. •

**L. Dade Lunsford, MD**

*Lars Leksell Professor*

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(All amounts: Up to \$1,000, except as noted.)

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### Pitt Alumni, Faculty Train Russian Colleagues

**Mark McLaughlin, MD**, a 1999 graduate of the University of Pittsburgh's neurological surgery residency program, organized and directed a neurosurgery symposium in St. Petersburg, Russia, on August 15-17, 2005. The symposium, entitled "Advances in Brain and Spine Surgery: Technology and Care," was dedicated to improving patient care in a country burdened with a challenged health care system and limited resources for neurosurgical training. Over 100 Russian neurosurgeons attended the event.

The symposium was the second organized in Russia by Dr. McLaughlin who has long ties of friendship and collaboration with Russian neurosurgeons, particularly Dr. Yuri Shulev, chief of neurosurgery at the Medical Academy of Postgraduate Studies, whom he first met in 1997. At that time, Dr. McLaughlin saw the great need for support and training in the Russian neurosurgical community.

**P. David Adelson, MD**, pediatric neurosurgeon at Children's Hospital of Pittsburgh and vice chairman of research for the department, served as guest faculty at the symposium. Other internationally recognized neurosurgeons who taught at the symposium included Drs. Edward Benzel, Art Day, Richard Fessler, Regis Haid, Peter Jannetta, Hae-Dong Jho, Iain Kalfas, and Volker Sonntag.

### New Research Grants

"Protein Phosphatase 2B Signaling Mechanism in TBI," **C. Edward Dixon, PhD**, National Institute of Neurological Disorders and Stroke, \$1,648,800.

"Isolation of Selective Microvascular Endothelial Cell Targets Critical for Brain Tumor Angiogenesis," **Kevin Walter, MD**, American Brain Tumor Association, \$50,000.

"HSV-1 Convection-Enhanced Delivery and Chemoradiosensitivity Enhancement in a Human Glioma Model," **Costas Hadjipanayis, MD, PhD**, American Brain Tumor Association, \$70,000.

### Media

• **A. Leland Albright, MD, Amin Kassam, MD, L. Dade Lunsford, MD, Joseph Maroon, MD, and Ian Pollack, MD**, were named among this area's top doctors in a national survey published locally in the May issue of *Pittsburgh Magazine*.

• **William Welch, MD**, was interviewed on the WTAE-TV Evening News (Pittsburgh), April 7, about his work with Dynesys®, a revolutionary new spine stabilization system utilized in the treatment of patients with lower back and leg pain.

• The minimally invasive technique of accessing the brain through the nose performed by physicians **Carl Snyderman, MD**, and **Dr. Kassam**, was also featured on WTAE-TV, February 15.

### Visiting Lectures

• **Dr. Lunsford** was a guest speaker at the Japanese Gamma Knife Society in Tokyo on February 1. Dr. Lunsford was also the visiting lecturer at the Nakamura Memorial Hospital in Sapporo, Japan on February 6.

• **Dr. Kassam** served as a guest faculty member at the "Minimally Invasive Surgery and Endoscopic Skull Base Dissection" course in Toronto, February 2-3 and at the "4th Annual Otolaryngology Update" meeting in Toronto on February 4. Both events were sponsored by the University of Toronto.

• **Douglas Kondziolka, MD** was a visiting professor at Northwestern University on February 10 and at the University of Medicine and Dentistry, New Jersey (UMDNJ) on March 8.

### Awards

The paper "Injury During Pregnancy: A Neglected Child Injury Issue," coauthored by CIRCL director **Hank Weiss, PhD**, was awarded top prize at The International Society for Child and Adolescent Injury Prevention" meeting in Durban, South Africa, April 5-6.

### Personal Congratulations

• **Cheryl Rodgers**, Gamma Knife nurse, took a one-month leave of absence to do humanitarian work in the tsunami-damaged area of Sri Lanka.

• Baby boy (Richard Matthew, November 4) to **Dr. Adelson**, and wife Barbara; baby boy (Travis Martin, February 8) to **Ed Schaffer**, physician assistant, and wife Gina; baby girl (Caroline Olivia, February 10) to **Dave Atteberry, MD**, PGY-5 resident, and wife Carla.

### Promotion

**Jeff Bost, PA-C**, was promoted to clinical instructor.

### Welcome

**Jadish Bhatnager, ScD**, clinical associate professor; **Linda Peter**, physician assistant; **Carrie Bisogni**, neurophysiology technologist; **Sherman Culver**, research assistant to C. Edward Dixon, PhD; **Jeremy Henchir**, research assistant to Dr. Dixon; **Qiwei Han**, research assistant to Paola Grandi, PhD; **Debroah Michel**, secretary to Dr. Adelson; **Aalap Shah**, research assistant to Dr. Walter; **Theodore J. Spinks, MD**, pediatric fellow; **Faith Lewis**, pediatric secretary; **Kirsten Stalder**, Tri-State RN; **Tao Song**, CIRCL graduate student researcher; **Kathy Higgins, RN**, clinical trials manager for Dr. Welch, and Peter Gerszten, MD; **Kathy Smith**, nurse coordinator for Richard Spiro, MD.

### Calendar of Events

• May 10: **Visiting Professor Lecture Series**. "Project Shunt: The University of Michigan Department of Neurosurgery Goes to Guatemala," **Karin Muraszko, MD**, professor and chair of the Department of Neurosurgery at the University of Michigan. (UPMC Presbyterian, Suite B-400, 4:00 p.m.) Dr. Muraszko is the first woman to chair a neurosurgery department in the United States.

• June 2-3: **Minimally Invasive Endoscopic Surgery of the Cranial Base and Pituitary Fossa Course**. Presentation of minimally invasive techniques for endoscopic surgery of the cranial base and pituitary fossa. Call (412) 647-6358 for more information.

• June 5-9: **Principles and Practice of Gamma Knife Radiosurgery**. For neurosurgeons, radiation oncologists and medical physicists interested in Gamma Knife radiosurgery education. This course will also be offered July 10-14. Call (412) 647-7744 for more information.

• September 11-13: **Gamma Knife Radiosurgery Training for Nurses**. For nurses and other allied health care personnel interested in providing clinical care for patients undergoing Gamma Knife radiosurgery. Call (412) 647-7744 for more information •



Department of Neurological Surgery  
University of Pittsburgh Medical Center  
UPMC Presbyterian/Suite B-400  
200 Lothrop Street  
Pittsburgh, PA 15213  
(412) 647-3685  
neuroinfo@upmc.edu

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## Artificial disc studied as alternative to cervical fusion

The Department of Neurological Surgery at the University of Pittsburgh has been selected to be one of twenty sites for an Food and Drug Administration study of a new device seen as an alternative to cervical fusion for the treatment of certain types of chronic neck pain as well as arm pain.

Safety data has been acquired based on hundreds of patients in South Africa implanted with the Kineflex|C™ Spinal System. The FDA has granted an investigational device exemption (IDE) approval to conduct a pivotal study utilizing this new disc, with study patients to be randomized equally to the disc or to anterior cervical disc fusion (ACDF) surgery. There are currently no cervical artificial discs approved by the FDA in the United States.

Peter C. Gerszten, MD, and William C. Welch, MD, are evaluating the Kineflex|C artificial disc for the treatment of arm pain and neck pain caused by degenerative disc disease (DDD). The neurosurgeons will

be comparing the Kineflex|C to the more standard cervical discectomy and fusion in a randomized clinical trial. The goal of the artificial disc is to preserve motion, while minimizing or eliminating pain. The preservation of motion at the diseased segment, as opposed to fusion, is believed to prevent further degeneration of adjacent disc levels.

The Kineflex|C artificial disc is a three-component modular system, manufactured by SpinalMotion of Sunnyvale, CA. The endplates and mobile core are of cobalt-chrome-molybdenum (as used in hip and knee implants), and the bone-contact surfaces of the endplates are coated with a plasma spray of titanium (for bone on-growth). Animation of the disc can be viewed on SpinalMotion's website at [www.spinalmotion.com](http://www.spinalmotion.com).

If you are interested in further information about requirements for patients' participation in the study, please contact Dr. Gerszten, or Pat Karausky, the trial's clinical study coordinator at: (412) 802-3229.

## Welch lecture to inaugurate Peter E. Sheptak Chair



William Welch, MD, (L) chief of neurosurgery at UPMC Presbyterian and director of the UPMC Spine Services Division, will provide a lecture on 'Regenerative Spine Surgery,' May 18 at 4:30 p.m. in 2500 Posvar Hall, to mark his appointment as the Peter E. Sheptak Chair in Neurosurgery at the University of Pittsburgh. The chair honors the 30+ year career of Peter E. Sheptak, (R), vice-chairman of clinical affairs for the department. A wine and cheese reception will follow the lecture. For more information, please call (412) 647-0990.