UNIVERSITY of WASHINGTON SCHOOL of MEDICINE

The Montlake Cut



A Newsletter from the Department of Neurological Surgery October 2009, Volume 1, Number 4



Autumn on the Montlake Cut



Bob Rostomily, MD, with nurse Janet

Team Approaches to Tumors

It is not news to anyone in the medical profession that the treatment of many brain tumors remains a work in progress. While the surgical management of most benign neoplasms of the nervous system has made steady advances since Victor Horsley and then Cushing were first bold enough to attempt the operations, a cure for malignant tumors has always been just around the corner—for the past 100 years!

The Department of Neurological Surgery has, as part of its mission, a major commitment to improved understanding of a broad spectrum of pediatric and adult neoplasms. Attacking these problems most profitably requires both clinicians dedicated to caring for afflicted patients, and sophisticated research efforts aimed at examining the cellular basis of the pathology. A collaborative approach that involves basic scientists and clinicians investigating the same diseases is a fundamental tenet to the unique work now being done at UW Neurological Surgery. This effort spans 4 institutions (UW Medicine -UWMC/HMC, Seattle Children's and the Fred Hutchinson Cancer Institute), together forming the Seattle Cancer Care Alliance (SCCA), and incorporates the work of 7 Departments. The SCCA enjoys over 10 million dollars of extramural funding directed at "finding the cure".

Leading the clinical assault on tumors in adults at UW Medical

Center, Professor Daniel Silbergeld and Associate Professor Robert Rostomily combine to run an active tumor surgery service, operating on about 300 patients a year. Dan treats primarily pituitary and glial tumors, often employing the technique of awake cortical mapping. Bob specializes in acoustic neuromas and other skull base lesions, working with a team that includes neuro-otologists and ENT surgeons. In addition, Drs. Rostomily and Jason Rockhill, MD, PhD, (Assistant Professor, Radiation Oncology), with assistance from Assistant Professor Adam Hebb and Emeritus Professor Robert Goodkin, supervise the radiation therapy of an



Dan Silbergeld, MD

additional 180 patients at the UW Gamma Knife Center located at the Harborview campus.

...over 750 patients a year are treated for brain tumors throughout the department.



Drs. Browd, Ko (top), Ellenbogen, Ojemann, Avellino (middle), Hebb (bottom)



Expression of mitochondrial targeted green fluorescent protein (EGFP) in NeuN-positive retinal ganglion cells demonstrates that neurons contain small, punctate or tubular mitochondria. (image from R. Morrison lab)

Professor and Vice Chair Laligam Sekhar and his team operated on more than 200 patients last year referred to Harborview from 9 countries and 38 states with various neoplasms at the cranial base. A pioneer in skull base surgery, Dr. Sekhar is currently the President of the World Federation of Skull Base Societies. Assistant Professor Louis Kim is also surgically active at the skull base. Department Chair Rich Ellenbogen adds an additional 50 minimally invasive endoscopic brain operations a year at Harborview, including surgery for intraventricular, pituitary, pineal region, and posterior fossa tumors in adults.



Laligam Sekhar, MD

Professors Ellenbogen, Jeffrey Ojemann and Assistant Professor Sam Browd at Seattle Children's Hospital treat roughly 100 kids with CNS neoplasms yearly. In total, over 750 patients a year are treated for brain tumors throughout the department. All of these faculty members are actively working both in their own labs, and in cooperation with other clinicians and basic scientists in many other departments and schools on all 4 campuses at the UW.

Although I won't describe them all, below are a few of the multidisciplinary efforts. Professor John Silber's lab (with Associate Professor Michael Bobola) focuses on DNA repairmediated alkylating agent resistance in human gliomas. Currently, these chemotherapeutic agents plus radiation modestly improve response and survival in patients with malignant gliomas. The long-term objective in the Silber lab is to define the contribution DNA repair makes to resistance such tumors demonstrate against chemotherapy, and to define strategies to combat it. Promising targets have been identified, and studies are underway that focus on cytotoxic abasic sites, which are the most abundant lesions produced by alkylating agents.

Professor Richard Morrison's lab is approaching the tumor problem down the adjacent avenue of programmed cell death and proteomics. Cells that are damaged but not killed undergo the initiation of an energy dependent process that requires turning on a genetically programmed pathway called apoptosis. As opposed to necrosis, apoptosis involves the orderly breakdown of a cell with minimal inflammation. However, in the end, the cell is just as dead. Morrison and colleagues aim to find methods that block these biochemical pathways. All cells employ surveillance mechanisms to identify and repair DNA damage. One of these is the p53 tumor suppressor gene. In the Morrison lab, transduction pathways associated with p53 induced cell death are being characterized in the hope that interrupting the function of the gene in this process may protect cellular viability around tumors. In addition, Dr. Morrison just obtained a prestigious NIH Center grant in Proteomics (supporting 18 institutions throughout the country) aimed at better understanding downstream effects of the genetic aberrations.

the Mourad lab is now concentrated on using bioengineering principles in diagnostic and therapeutic ultrasound.

> Drs. Rostomily and Horner are examining mechanisms that contribute to glioma invasion, age-related malignancy and treatment resistance.

One of the most interesting and unusual avenues into brain tumor research is an R0-1/P0-1 NIH funded Nanotechnology effort to study the "tumor paint" It's a little hard to believe that a mathematical physicist and senior scientist at the Applied Physics Lab would also find work in a department of neurological surgery, but Associate Professor Pierre Mourad has done just that. Beginning from a thesis on atmospheric turbulence, segueing to medical acoustics, the Mourad lab is now concentrated on using bioengineering principles in diagnostic and therapeutic ultrasound. Research highlights include: using ultrasound to disrupt the blood-brain barrier, treat peripheral nerve injury, and delivery of medications via an ultrasound-activated implanted reservoir. Other applications under investigation by these novel methods involve the induction of necrosis and apoptosis by ultrasound and the development of a non-invasive intracranial pressure monitor.

In addition to his clinical practice, Dr. Rostomily's NIH funded lab works closely with Phil Horner, PhD, Associate Professor, a stem cell biologist in the Neurological Surgery Department. Together they are examining mechanisms that contribute to glioma invasion, agerelated malignancy and treatment resistance. Neural stem and progenitor cells are the presumed cells of origin for these tumors. Recent work has demonstrated specific age-related changes occur in stem cells, including increased malignancy after transformation compared with their young adult counterparts. Work in the Rostomily lab is directed at understanding these changes.

One of the most interesting and unusual avenues into brain tumor research is an R0-1/P0-1 NIH funded Nanotechnology effort to study the "tumor paint", chlorotoxin Cy5.5 (patent pending), which occurred with the help of Chief Resident Patrik Gabikian. He was part of a team working in the labs of Professors Jim Olson (Pediatrics/Oncology/Fred Hutch), Miqin Zhang (Engineering/ Neurological Surgery) and Rich Ellenbogen (Neurological Surgery). These investigators are investigating focused therapy for brain tumors through molecular imaging techniques employing "designer" nanoparticles that expose brain tumors (through the skin and skull of animals) using the infrared spectrum of light and MRI.

Together, these clinicians and basic scientists are united as the multi-disciplinary Neuro-oncology team investigating tumors in both children and adults. The link below will connect you to several open clinical research studies, as well as contact information. For patients who are out of other options, such clinical trials are sometimes appropriate. Open studies include a phase II trail using PTK-787 to treat recurrent or progressive meningiomas, a phase II trial treating high-grade recurrent gliomas with Bendamustine, a phase III study comparing several treatments of recurrent glioblastoma, and a phase I-II study that employs autologous chemo-protected stem cells and chemotherapy in patients with malignant gliomas. *http://depts.washington.edu/neurosur/trials/tumors.html*

Personal Preferences in Neurosurgery:

In 2003, Emeritus Clinical Professor, David Pithkethly, M.D. created a teaching tool for residents, called "Personal Preferences in Neurosurgery" which can now be downloaded free. This simple illustrated guide is an instructional description of how to do basic neurosurgical procedures that trainees in quaternary medical centers sometimes don't see much, but will in other settings. This manuscript can be downloaded here:

http://depts.washington.edu/neurosur/residency/academics.html#preferences

Back to the VA



Misha Gelfenbeyn, MD



Anthony Avellino, MD



Michel Kliot, MD



Rich Ellenbogen, MD

For years, our department ran the neurosurgery service at the Veterans Administration Puget Sound Health Care System on Beacon Hill. Most of those readers who were residents more than fifteen years ago remember the pale green ward and lines of back pain patients in clinic. For reasons related to the manpower of the residency and work-week limitations, we were forced to reduce our presence at the VA for about 5 years.

Then, Misha Gelfenbeyn finished his second neurosurgical residency (see Volume 1, #3). The Division of Neurosurgery in the Department of Surgery at the Puget Sound VA Health Care System has recently hired Misha to complement Michel Kliot, Tony Avellino and Rich Ellenbogen who are now there part-time.

In addition, the service has added two physicians assistants and a nurse practitioner. Together, this staff evaluate and treat veterans with peripheral nerve problems and spine disease. We expect that this service will expand and grow over the coming years to become a referral center for other VA Hospitals in the region.

Fangyi Zhang, MD

Back to HMC

Dr. Fangyi Zhang is the newest appointment to our faculty as Assistant Professor of Neurological Surgery and attending neurosurgeon at the University of Washington School of Medicine. Dr. Zhang received his medical degree in 1986 at Capital University of Medical Sciences in Beijing, China, and then did a five-year neurosurgical residency at the Beijing Neurosurgical Institute in China.

In 1991, Dr. Zhang came to the United States to do research in cerebrovascular biology and stroke in the Department of Neurology at the University of Minnesota. Seven years later, from 1998-2003, he repeated his clinical training at the University of Texas Health Science Center in San Antonio, Texas.

He then joined the University of Washington Department of Neurological Surgery as a senior resident and then chief from 2003-2005, followed by a year as a Spine Surgery Fellow in both Orthopaedic Surgery and Neurological Surgery, also at UW. Dr. Zhang is *very* well trained.

From 2006 to 2009, Dr. Zhang practiced in Houston, Texas with a faculty appointment as an Assistant Professor in the Department of Neurosurgery at the University of Texas Health Sciences Center. At the University of Washington and Harborview Medical Center, he focuses on complex and minimally invasive spinal surgery in the management of degenerative spine disorders, as well as the management of traumatic spine and traumatic brain injuries. We are all delighted that Fangyi Zhang has returned to join us at UW Medicine. He is a first-class addition.

Hike to the Heavens-year two

For the second time, Assistant Professor Louis Kim has organized the departmental "hike to the heavens" on the Olympic peninsula. This year, there were 14 hikers and one pregnant observer, making the event a huge success for faculty, residents, wives, and friends. Part of the glory of living in the Pacific Northwest, of course, is easy access to some of the most beautiful and still natural regions of the country.





After







~ Baby Book ~

Our younger faculty members and residents are very, very good at a lot of things, but they seem especially proficient at producing baby daughters! Here is the work of the past few months.



Azalia Tashman Kim, born August 17 to Assistant Professor Louis Kim and his wife Aylin, is their first child.

Assistant Professor Trent Tredway and his wife Annisa are the parents of their first child, daughter Zayna Alaina, born August 28.





Assistant Professor Virany Hillard and her husband Brooke had a second daughter, Nuwa Arwen, born on June 12.



As previously reported, Assistant Professor Adam Hebb and his wife Shauna Runchey also had a daughter, Catherine, born last January 24.

Also noted previously, Chief Resident Tim Lucas and his wife Patricia produced the fifth new departmental daughter, Sophia, on March 28



The Montlake Cut is a quarterly newsletter published by the Department of Neurological Surgery at your University of Washington School of Medicine. We hope to keep the neurosurgeons in the entire WWAMI Region informed about resources available through the university system and, just as importantly, to learn from you any information about your lives and practices that you care to provide. Especially for the graduates of our program, as well as former staff and faculty, we welcome e-mail or letters describing your current activities and reminiscences about your time at UW. We will continue to feature stories about former staff members of the department in the "Where Are They Now?" section, along with news of current faculty, staff and residents.

We sincerely hope that the newsletter will evolve into a collegial method for sharing news and information electronically throughout the region. Please contact us at the addresses below. If you wish not to receive the Montlake Cut, please let us know and we'll remove your name from the distribution list.

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