

Brain Tumor Center | 2009–2010 Progress Report

MEMORIAL SLOAN-KETTERING CANCER CENTER

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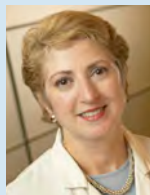
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BRAIN TUMOR CENTER MEMBERS

Our multidisciplinary team of doctors includes treating physicians, diagnostic and supportive care professionals, and accomplished scientists across eight departments and seven programs.

NEUROLOGY/NEURO-ONCOLOGY



Lisa DeAngelis, MD



Edward Avila, DO



Xi Chen, MD, PhD



Milan Chheda, MD



Denise Correa, PhD



Igor Gavrilovic, MD



Adilia Hormigo, MD, PhD



Thomas Kaley, MD



Andrew Lassman, MD



Ingo Mellinghoff, MD



Craig Nolan, MD



Antonio Omuro, MD



Gavril Pasternak, MD, PhD



Jerome Posner, MD

NEUROSURGERY



Philip Gutin, MD



Mark Bilsky, MD



Cameron Brennan, MD



Eric Holland, MD, PhD



Mark Souweidane, MD



Viviane Tabar, MD

PEDIATRIC NEURO-ONCOLOGY



Oren Becher, MD



Ira Dunkel, MD



Stephen Gilheeny, MD



Yasmin Khakoo, MD



Kim Kramer, MD



David Lyden, MD, PhD

RADIATION ONCOLOGY



Kathryn Beal, MD



Timothy Chan, MD, PhD



Suzanne Wolden, MD



Yoshiya Yamada, MD

NEURORADIOLOGY



Hedvig Hricak, MD, PhD



Timothy Akhurst, MBBS



Michelle Bradbury, MD, PhD



Sofia Haque, MD



Andrei Holodny, MD



Sasan Karimi, MD



George Krol, MD



Eric Lis, MD



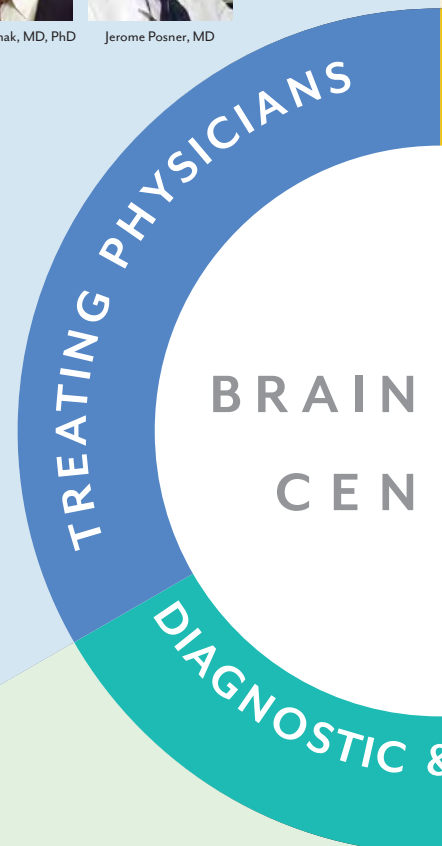
John K. Lyo, MD



Hilda Stambuk, MD



Robert Young, MD



MOLECULAR PHARMACOLOGY & CHEMISTRY



Luca Cartegni, PhD



Hakim Djaballah, PhD



Michael McDevitt, PhD



Stephen Nimer, MD



Jerome Posner, MD



Neal Rosen, MD, PhD

CANCER BIOLOGY & GENETICS



Joan Massagué, PhD



Robert Benezra, PhD



Eric Holland, MD, PhD



Johanna Joyce, PhD



Anna Kenney, PhD

COMPUTATIONAL BIOLOGY



Franziska Michor, PhD



MOLECULAR BIOLOGY



Andrew Koff, PhD



John Petrini, PhD

NEUROPATHOLOGY



Jason Huse, MD, PhD



Marc Rosenblum, MD

CELL BIOLOGY



Xuejun Jiang, PhD



Marilyn Resh, PhD

NEUROSURGERY



Dolores Hambarzumyan, PhD



Viviane Tabar, MD

SURGERY



Bhuvanesh Singh, MD, PhD

DEVELOPMENTAL BIOLOGY



Alexandra Joyner, PhD



Songhai Shi, PhD



Lorenz Studer, MD

HUMAN ONCOLOGY & PATHOGENESIS PROGRAM



Charles Sawyers, MD



Cameron Brennan, MD



Timothy Chan, MD, PhD

PSYCHIATRY & BEHAVIORAL SCIENCES



Timothy A. Ahles, PhD



William S. Breitbart, MD

EPIDEMIOLOGY & BIOSTATISTICS



Jonine Bernstein, PhD



Sara Olson, PhD



Katherine Panageas, DrPH



Ingo Mellingerhoff, MD

SPOTLIGHT

Viviane Tabar, MD

Viviane Tabar is a neurosurgeon with a broad range of interests in the clinic, the operating room, and the laboratory. Since joining the Department of Neurosurgery in 1998, she has cared for patients with benign tumors such as meningiomas and pituitary adenomas, those with aggressive malignant diseases such as glioblastomas and astrocytomas, and patients with brain metastases. She also conducts laboratory research focused on the study of human stem cells and their potential role for treating brain disorders. We asked her about the new Pituitary Tumor Center she established at Memorial Sloan-Kettering and her research goals.

What drove you to choose neurosurgery as a career?

The brain, because it is a very sophisticated organ. It defines who people are. There is a lot that remains to be discovered about the brain, so it provides a lifelong, continuously fascinating challenge.

What are pituitary tumors, and how do they affect patients' lives?

Pituitary tumors are benign tumors of the pituitary gland, the master gland in the body. They occur in about one in five people. While most of them don't cause any problems, some of them cause hormonal imbalances such as gigantism. Other patients may experience voice changes, trouble sleeping, vision problems, headaches, and difficulties with menstruation or fertility. So even though these tumors are not life-threatening, they can impair quality of life.

Most patients live a long time after they receive treatment. Because their life expectancy is long, their quality of life after treatment is paramount.

Why did you decide to create the Pituitary Tumor Center, and what benefits does it offer to patients?

Patients with pituitary tumors have a wide variety of needs and usually have to see a team of professionals for evaluation and treatment, including an endocrinologist, an ophthalmologist, and a neurosurgeon. It could take months for patients to receive a recommendation for their care. Through the Pituitary Tumor Center, Memorial Sloan-Kettering has the manpower, technology, and expertise to offer all of these services in one convenient location. Patients can often see all of their doctors on the same day, which is especially helpful for patients coming from other states or countries.



Patients come here because they know they're getting the excellent care for which Memorial Sloan-Kettering is known. We've gone from treating three or four patients with pituitary tumors per year to about 200.

I like treating these patients because they widen my horizon as a physician. It's great to be able to offer them multidisciplinary care that is hard to find elsewhere and is the best way to manage their problem.

What kinds of advances at MSKCC are improving the care of patients with pituitary tumors?

An important advance has been the use of intra-operative MRI, which allows us access to do live imaging during surgical removal of the tumor. This is critical, because when you remove the tumor, there is a significant shift in the topography of the brain: the gland's position changes and the relationship of residual tumor to the surrounding structures also changes. It also gives us the ability to look for very small amounts of residual tumor tissue while avoiding delicate structures nearby, such as the optic nerves and the carotid arteries. It's important to remove as much tumor as possible while preserving the gland itself, so that patients won't need a lifetime of hormone therapy. We are probably the only center in the United States doing pituitary surgery routinely in a high-field MRI suite.

Can you tell us about your research on stem cells?

It was once thought that you were born with a certain number of brain cells, and those were

the cells you would have for life — you would never grow new ones. But we now know that stem cells that mature into new nerve cells exist in the brain.

Recently, we've learned how to turn adult skin cells in the laboratory into embryonic stem cells. In my research, I am studying how to harness this technology to repair brain damage due to degenerative disease such as Parkinson's or Lou Gehrig's disease, or due to other insults such as radiation. These stem cells can be derived from each individual patient, and therefore cannot be rejected as foreign. They can also help us model disease in the lab in our search for new therapies.

What do you see as your greatest challenge?

I want to do the best job I can as both a physician and a scientist. Malignant brain tumors remain very difficult to treat successfully. Five years from now, I'd like to be able to offer more effective treatments for my patients. I hope we hit an exponential phase in our research accomplishments. I feel sometimes we're close, but we're not there yet.

How does the collaborative atmosphere at Memorial Sloan-Kettering further your work?

This is a place teeming with smart people. I collaborate not only with other clinical members of the Brain Tumor Center, but also molecular biologists, stem cell biologists, developmental biologists, computational biologists, and others. Science is a collaborative endeavor. You can't do it alone, and the many talented people here provide the right combination to further our research.



BTC-AFFILIATED CENTERS

PITUITARY TUMOR CENTER

Appointments: 212-639-3935

The Pituitary Tumor Center, established in 2007 by Dr. Viviane Tabar, combines the expertise of the departments of Neurosurgery, Endocrinology, Neuro-Ophthalmology and Radiation Oncology. Dr. Tabar, a researcher and neurosurgeon, understood that, despite being a cancer center, Memorial Sloan-Kettering also had a unique capability for treating benign pituitary tumors, also known as adenomas. Before the center was created, Memorial Sloan-Kettering had treated only three or four cases of pituitary adenoma each year, usually in patients who already were being treated for some type of cancer. Now Memorial Sloan-Kettering sees about 200 patients with pituitary tumors each year, with most of those tumors being benign.

NEUROSURGERY

Viviane Tabar, MD

RADIATION ONCOLOGY

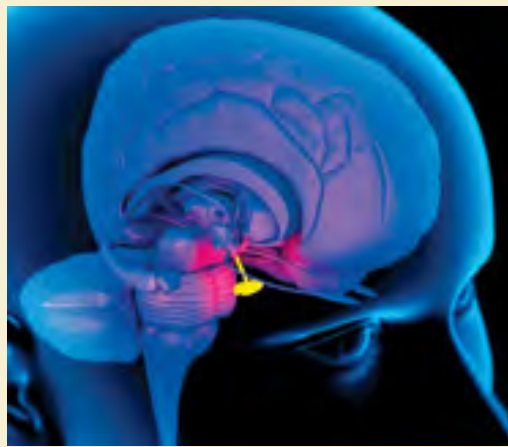
Kathryn Beal, MD

ENDOCRINOLOGY

Monica Girotra, MD

NEUROLOGY

Marc J. Dinkin, MD



SPINE TUMOR CENTER

Appointments: 212-639-6506

The Spine Oncology Team at Memorial Sloan-Kettering Cancer Center is a multidisciplinary group of approximately 15 doctors who closely collaborate in the treatment of patients with primary and metastatic tumors that come to the Spine Clinic. This group approach draws on physicians from the departments of Neurosurgery, Neurology, Neuroradiology, Orthopaedic Surgery, Radiation Oncology, Interventional Radiology, Anesthesiology, and Rehabilitation Medicine to ensure that patients who need several different therapies to treat their cancer will receive the safest and most effective combination. The Spine Clinic treats more than 1,400 patients each year.

NEUROSURGERY

Mark Bilsky, MD

RADIATION ONCOLOGY

Yoshiya Yamada, MD

Brett Cox, MD

NEURORADIOLOGY

George Krol, MD

Eric Lis, MD

ORTHOPAEDIC SURGERY

Edward Athanasian, MD

Patrick Boland, MD

NEUROLOGY

Edward Avila, DO

Xi Chen, MD, PhD

Sonia Sandhu, DO

INTERVENTIONAL RADIOLOGY

Pierre Gobin, MD

Athos Patsalides, MD

ANESTHESIOLOGY

Kenneth Cubert, MD

Amitabh Gulati, MD

REHABILITATION MEDICINE (PHYSIATRY)

Christian Custodio, MD

Jonas Sokolof, DO

Michael Stubblefield, MD

PHYSICAL SCIENCES-ONCOLOGY CENTER

EVOLUTIONARY DYNAMICS OF BRAIN, LUNG AND HEMATOPOIETIC TUMOR

In October 2009, a team of eight researchers, six of whom are at Memorial Sloan-Kettering, received an \$11 million, five-year grant from the NCI to form one of 12 Physical Sciences-Oncology Centers (PS-OCs) in the United States. The PS-OCs bring together experts from physics, mathematics, chemistry, engineering, and oncology to better understand the physical and biological principles of the emergence and behavior of cancer. The PS-OC at Memorial Sloan-Kettering, focused on mathematics and computational biology, is led by evolutionary biologist Franziska Michor in the Computational Biology Program. Dr. Michor, who arrived at the Sloan-Kettering Institute in 2007, uses the tools of applied mathematics and evolutionary biology to study cancer initiation, progression, and resistance to treatment.

COMPUTATIONAL BIOLOGY

Franziska Michor, PhD

Grégoire Altan-Bonnet, PhD

Chris Sander, PhD

ORGANIZATION AND INFRASTRUCTURE

Desert Horse-Grant

Mithat Gonen, PhD

CANCER BIOLOGY, ONCOLOGY, AND SURGERY

Maribel Vazquez, PhD

Eric Holland, MD, PhD

Ross Levine, MD

Ingo Mellinghoff, MD

William Pao, MD, PhD

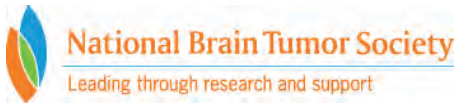
OUTREACH – 2009 PATIENT CONFERENCE

On April 17, 2009, nearly 200 people attended “Let’s Talk about Brain Tumors,” a **patient conference** co-sponsored by the Brain Tumor Center at Memorial Sloan-Kettering and the National Brain Tumor Society.



“I’ve always found that if you ask the doctors at Sloan-Kettering a question, you get an honest answer.”

– Minna Immerman
Patient’s Wife



Regional Conference

learn • discuss • connect

Friday, April 17th, 2009

8:30 AM - 4:15 PM
430 East 67th Street (Rockefeller Research Laboratories)
New York, NY 10065

For Questions and to Register Call:
NBTS Patient Services
Line 800 934 2873 or visit our website,
www.brainumor.org

Gain up-to-date information on your own or a loved one’s diagnosis while sharing experiences and making connections with others in the brain tumor community. Join National Brain Tumor Society and The Brain Tumor Center at Memorial Sloan-Kettering Cancer Center for our Regional Conference.

This full day event brings brain tumor experts together, with you.

By attending you will:

- learn:** about the latest advancements in standard and experimental therapies, integrative medicine, coping strategies, and more.
- discuss:** your questions with leading experts.
- connect:** with other patients, survivors, and caregivers.



*“This **patient event** is a wonderful opportunity to provide both education for our patients and their families as well as a forum for them to meet with our staff informally and to share their personal stories and achievements with each other.”*

– Lisa M. DeAngelis, MD

“There are always so many questions that need to be answered with a brain tumor diagnosis. It is so reassuring to hear from others who are going through the same thing.”

– Regional Conference attendee



PATIENT HIGHLIGHTS

Three weeks before Colleen Fitzsimmon's (pictured right) 29th birthday, she had a seizure. A CT scan was recommended by her local doctor which showed a mass in her brain. After several opinions, she was referred to MSKCC. She consulted with Dr. Lisa DeAngelis who recommended surgery. It was during her first appointment with Dr. Philip Gutin that she told him she was training for the 2008 ING New York City Marathon. "He said that he couldn't see any reason for me not to do it." The five-hour-long procedure took place two weeks later, on August 7th. Dr. Gutin was able to remove the tumor, and the pathology report showed that Colleen had an oligodendroglioma, a rare, slow-growing tumor that begins in the cells that cover and protect nerve cells in the brain and spinal cord known as oligodendrocytes. She went home a few days later and was able to go back to her job as a physical therapist the following month. Soon after surgery, Colleen resumed her training schedule and was able to reach her goal of qualifying for a spot in the ING New York City Marathon. She took Dr. Gutin's advice and joined MSKCC's Fred's Team, choosing to earmark the money she raises for the Brain Tumor Center at Memorial Sloan-Kettering. "You think you're invincible," she says. "This has completely changed my life. It's a cliché to say, but this has changed my outlook on everything. I no longer get upset about the little things and don't take life for granted any more."



MSKCC Newsletter
Bridges: Connecting Cancer Survivors, Summer 2010

to not enjoy life and believe that there will be a tomorrow, and I say that because I know the human spirit is more powerful than the body or any disease."

The New York Times

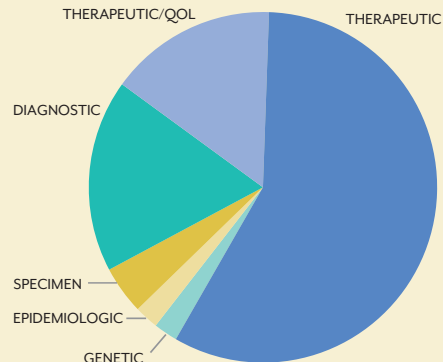


NY Times Magazine Ad
April 12, 2009

Matthew Peene was diagnosed with medulloblastoma at the young age of six. He was treated with three brain surgeries, chemotherapy, craniospinal radiation, and had a ventriculoperitoneal shunt placed in his brain for hydrocephalus. He became completely paralyzed on the left side. Through his "hard drive and the inspiration of family and friends" he began to walk again. Matthew expresses that his experiences in life have brought him to want to help cancer patients and anyone else who has any physical illness. "These doctors saved my life, and now it's my duty to help others like me." He celebrated his 21st birthday this year and is free of disease. He "beat the odds" and now plays guitar and is a goalie in a roller hockey league. His message to those diagnosed with cancer: "If one person reads this, what I would want them to know is that though things are bad it's never too bad

2009 BRAIN-RELATED PROTOCOLS & ACCRUALS

404 Patient Accruals



CLINICAL TRIALS ORIGINATING FROM MSKCC LABORATORIES

PI: OREN BECHER

Phase I Study of Perifosine with Temsirolimus for Recurrent Pediatric Solid Tumors
Opened: 01/13/2010

Phase I Study of Single Agent Perifosine for Recurrent Pediatric Solid Tumors
Opened: 10/20/2008

PI: ANDREW LASSMAN

Clinical and Molecular-Metabolic Phase II Trial of Perifosine for Recurrent/Progressive Malignant Gliomas
Opened: 05/09/2006

PI: KIM KRAMER

Phase I Study of Intrathecal Radio Immunotherapy Using 131I-8H9 for Central Nervous System/Leptomeningeal Neoplasms
Opened: 02/05/2004

Andrew Lassman, MD

Dr. Lassman came to Memorial Sloan-Kettering Cancer Center in 2001 to pursue a neuro-oncology fellowship, and he has been here ever since. He specializes in the medical treatment of patients with primary brain tumors and brain metastases. Recognizing that advances in medicine are made possible by translational research, Dr. Lassman designs and leads several clinical trials that bridge laboratory studies with patient care, evaluating new treatments for patients with brain tumors. We asked him about his work and what drives his professional pursuits.

What made you decide to study brain tumors and to care for patients with these diseases?

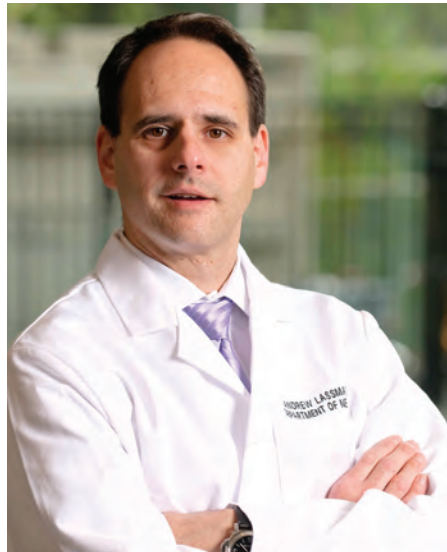
Even back in my days as an undergraduate at Yale University, I had an interest in molecular biology. I completed a dual bachelor's/master's degree program in molecular biophysics and biochemistry. The idea of learning about the body at the most fundamental level was not new to me; even as a kid, I liked figuring out how things worked, and I was into science and computers at a young age.

When I was in medical school and later in my residency, I became intrigued by the molecular biology of cancer, and was equally interested in the workings of the brain and the study of neurology. Brain tumors, especially glioblastomas, are incredibly complex diseases at the molecular level. I found that I could combine my interests in molecular biology, neurology, and cancer by focusing on the study and care of brain tumors. I set as my goal the cure of glioblastoma, which is notoriously stubborn and difficult to treat.

What made you decide to come to Memorial Sloan-Kettering?

This is the birthplace of neuro-oncology, started here by Dr. Jerome Posner decades ago. In addition to the excellent patient care for which this institution is known, I also had the opportunity to work with Dr. Eric Holland in his laboratory, where he has designed laboratory models to mimic and study a variety of brain tumors. This research stimulated my interest in the molecular biology of brain tumors and also led to fruitful collaborations with other investigators here in a variety of fields.

We have a biweekly seminar series and other meetings through the Brain Tumor Center that bring together basic science researchers and clinicians with the shared pursuit of



understanding and managing brain tumors. We communicate about our work, and also have the opportunity to expand our knowledge with presentations from speakers from both within and outside of the institution.

It takes a team approach to understand brain tumors, and a place like Memorial Sloan-Kettering has the breadth and depth that allow that to happen.

What do you think needs to happen for us to make progress against a cancer like glioblastoma?

Glioblastomas are molecularly complicated and are, in fact, at least three different molecular diseases. The advent of new targeted agents may revolutionize treatment, but there are several things we need to do to make progress.

First, we need to individualize therapy according to the molecular signature of each patient's tumor. The treatment of glioblastoma is not a "one-size-fits-all" approach. We have a huge effort under way here to learn how to select the most appropriate drugs for each patient's tumor, using novel drugs.

Second, we need to find out if the drugs we are using are actually penetrating into tumor tissue and hitting their targets.

Third, these tumors are so complex and driven by multiple molecular abnormalities. Therefore, rather than hoping that one drug with one target will be the answer, it will more likely take a drug

with multiple targets or multiple drugs with different targets. The treatment of other diseases, such as HIV/AIDS and multi-drug resistant tuberculosis, takes the same approach.

Finally, we need to use mouse models that accurately mimic human brain tumors. This is what Dr. Holland's lab is doing, with many advantages over other model systems used in the past. We've already begun two clinical trials of the drugs perifosine and temsirolimus in adult and pediatric patients with brain tumors based on promising data from mouse studies.

What keeps you going? What factors propel you in your work?

The interaction I have with my patients and their families means a lot. I value my ability to help people and relieve their suffering. I also value my interactions with my colleagues. The shared feeling of accomplishment when we make progress together is a great feeling. And the intellectual stimulation I get from taking what we learn in the laboratory and applying it to improving patient care makes this a great place to work. I also direct the neuro-oncology fellowship program, and enjoy teaching and mentoring the next generation of brain tumor specialists.

Do you still have a goal of curing glioblastoma?

I know glioblastoma remains a significant clinical challenge, but we're making progress. Rome wasn't built in a day; we have to be patient, and keep forging ahead. Although the average survival of patients with glioblastoma is woefully inadequate, we have learned how to identify patients with favorable prognostic factors — such as young age, ability to have the visible tumor removed surgically, and few or no symptoms — who have about a 30 percent five-year survival rate in a recent international clinical trial, and that is heartening. And the longer patients live, the more treatments will become available.

Looking back at my goal to cure glioblastoma, I'm realizing that maybe "cure" isn't the right word. When I was in medical school, people with AIDS lived just a few months on average; now people infected with HIV can live for decades with treatment. If we can learn how to treat brain tumors so that patients can live with them as a manageable condition for decades and have a good quality of life, in a sense, that is the start to a cure.

BTC SPECIALISTS IN THE NETWORK



Karen D. Schupak, MD
 Director of Radiation Oncology,
 Regional Care Network;
 Chief, Basking Ridge
 Radiation Oncology
 Appointments: 908-542-3100



Igor T. Gavrilovic, MD
 Neuro-oncologist
 Appointments: 908-542-3000



Craig P. Nolan, MD
 Neuro-oncologist
 Appointments:
 631-623-4100



Daphna Gelblum, MD
 Radiation Oncologist
 Appointments:
 631-623-4200



James Lee, MD
 Radiation Oncologist
 Appointments:
 631-623-4200



**NEURO-ONCOLOGY
 SOCIAL WORKER
 OF THE YEAR AWARD**



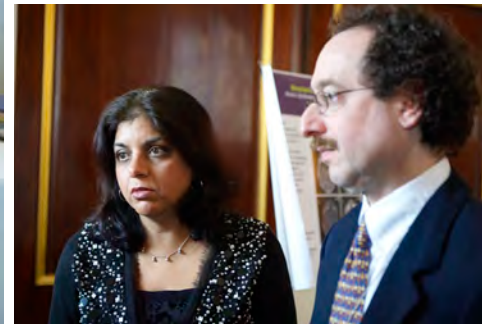
Melissa Stewart was presented with the “2010 Dennis Roth Neuro-Oncology Social Worker of the Year Award” by The Association of Oncology Social Work, sponsored by the National Brain Tumor Society. She was nominated by Lisa DeAngelis, MD, Chair, Department of Neurology, and Jane Bowling, DSW, Director, Department of Social Work, who described her as someone who “handles the most complex clinical situations with knowledge, excellent judgment, and a thorough approach to her interventions. As the caregiver burden is especially heavy for the families of brain tumor patients, she is able to transcend their infirmities and help the families cope at each stage of the disease continuum.”

BTC FAST FACTS FOR 2009

- The Department of Neurology had 546 new registrations and over 10,000 total visits.
- The Department of Neurosurgery performed over 700 procedures.
- The Department of Radiation Oncology consulted on the care of about 188 patients with brain tumors and 550 patients with brain metastasis.
- The Department of Pediatrics cared for an average of 60 patients with central nervous system tumors.

2010 FACULTY RETREAT

The Brain Tumor Center hosted its second retreat at the historic Metropolitan Club of New York on Friday, March 5, 2010. More than 60 people attended from ten clinical departments and six SKI programs as well as the external advisory board, the executive board, clinical and basic science fellows, and invited guests. Although the attendees spanned various areas of interest, there was a synergy across programs and departments, which could be attributed to the nearly three years of the BTC's efforts at promoting collaboration among these groups.



The day started with a short presentation on the new Physical Sciences-Oncology Center followed by the keynote address delivered by Paul Mischel, MD, an external advisory board member, speaking about targeted therapies. Progress made on previous BTC grant-funded projects was presented along with more than 25 posters from previous BTC grant winners as well as fellows from the clinical departments of Neurosurgery, Neurology, and Radiation Oncology, and the SKI programs of Cancer Biology & Genetics, Developmental Biology, Molecular Pharmacology, and Molecular Biology. The poster session

created an opportunity for junior members to share their work and receive advice from senior BTC faculty. A panel on molecular characterization was the focus of the afternoon session, which included BTC grant winners Jason Huse, MD, PhD, Department of Pathology, Cameron Brennan, MD, Department of Neurosurgery, Human Oncology & Pathogenesis Program; Andrew Lassman, MD, Department of Neurology; and Ingo Mellinghoff, MD, Department of Neurology, Human Oncology & Pathogenesis Program. Molecular characterization continues to be a research topic that many believe will lead

to more effective tailored treatments for patients.

The retreat ended with presentations by BTC grant winners Oren Becher, MD, of the Department of Pediatrics, on the modeling of brainstem gliomas and by Teodoro Pulvirenti, PhD, of the Cell Biology Program, on signaling in gliomas. Members of the external advisory board in attendance said they found the retreat to be worthwhile and in describing the event echoed one of the BTC's primary goals — bridging clinicians and basic scientists who are interested in brain cancer.

EDUCATION

BTC MEDICAL STUDENTS



The Brain Tumor Center has supported 19 medical students over the past two years. These students have been involved in a wide array of projects related to radiation response, effects of ABC transporter on BLI, models of diffusion tensor imaging, EEG abnormalities in the pediatric cancer population, and many more. Their mentors are spread over ten departments consisting of varied expertise. The BTC is committed to continuing the enrichment of medical students through the support of this program.

2009 MENTORS

DEPARTMENT OF NEUROLOGY

Lisa DeAngelis, MD
Edward Avila, DO

DEPARTMENT OF NEUROSURGERY

Mark Bilsky, MD

DEPARTMENT OF RADIOLOGY

Andrei Holodny, MD
Robert Young, MD

DEPARTMENT OF MEDICINE

Michael McDevitt, PhD

DEVELOPMENTAL BIOLOGY

Praveen Raju, MD, PhD
Alexandra Joyner, PhD

PEDIATRICS

Yasmin Khakoo, MD

RADIATION ONCOLOGY

Yoshiya Yamada, MD

2008 MENTORS

DEPARTMENT OF NEUROLOGY

Lisa DeAngelis, MD
Lauren Abrey, MD
Ronald Blasberg, MD
Adilia Hormigo, MD, PhD

DEPARTMENT OF NEUROSURGERY

Philip Gutin, MD
Viviane Tabar, MD

DEPARTMENT OF RADIOLOGY

Andrei Holodny, MD
Robert Young, MD

MOLECULAR BIOLOGY

John Petrini, PhD

MOLECULAR PHARMACOLOGY & CHEMISTRY

Luca Cartegni, PhD

2009–2010 BTC SEMINAR SERIES

2010 SPEAKERS

BTC MEMBERS

Dr. John Petrini, Molecular Biology
Dr. Timothy Chan, HOPP, Radiation Oncology
Dr. Xuejun Jiang, Cell Biology
Dr. Lorenz Studer, Developmental Biology
Dr. Stephen Nimer, Molecular Pharmacology & Chemistry
Drs. Jonine Bernstein and Sara Olson, Epidemiology & Biostatistics

EXTERNAL:

Dr. Robert Wechsler-Reya, Duke University
Dr. Ann Chambers, London Health Sciences Centre
Dr. Michael Taylor, Hospital for Sick Children
Dr. Michael Cooper, Vanderbilt University Medical Center
Dr. Nancy Tarbell, Harvard Medical School

2009 SPEAKERS

BTC MEMBERS

Dr. Ingo Mellinghoff, HOPP, Neurology, Facilitator
Dr. Viviane Tabar, Neurosurgery

Dr. Oren Becher, Pediatrics

Dr. Luca Cartegni, Molecular Pharmacology & Chemistry

Dr. Alexandra Joyner, Developmental Biology

Dr. Jason Huse, Pathology

Dr. Robert Benezra, Cancer Biology & Genetics

Dr. Anna Kenney, Cancer Biology & Genetics

EXTERNAL SPEAKERS

Dr. Steven Rosenfeld, Columbia University

Dr. Charles Stiles, Dana Farber Cancer Institute

Dr. Tracy Batchelor, Dana Farber/Harvard Cancer Center

Dr. Claudia Fischbach-Teschl, Cornell University

Dr. William Parsons, Baylor College of Medicine

Dr. Karen Cichowski, Brigham & Women's Hospital

Dr. Kenneth Adalpe, MD Anderson Cancer Center

Dr. Robert Blelloch, University of California, San Francisco

Dr. Daniel Turnbull, New York University

**54 TOTAL SPEAKERS IN PAST
3 YEARS; 34 EXTERNAL**

Franziska Michor, PhD

Getting to the heart of how and why brain tumors develop is critical for designing new treatments to combat them. Franziska Michor is combining her knowledge of applied mathematics and evolutionary biology with the expertise of her collaborators at Memorial Sloan-Kettering and the extraordinary computational biology and research resources that the institution provides to predict how brain tumors such as gliomas arise, progress, and become resistant to treatment. Here she talks about the use of mathematical models to better understand cancer development, and how she came to lead the Physical Sciences-Oncology Center (PS-OC) which was established at MSKCC in October 2009.

Some people say they just don't have a head for math. Were you always good at math?

I am not sure I am that good at math now, but I have always liked it because it is very concrete — what's true once is true forever, and under any circumstance. Growing up in Austria, near Vienna, my father, a mathematician, would often do math games with us, so I had a great deal of exposure to it. I disagree that some people can't "get" math. I think we're all capable of understanding it, you just have to have patience and a good teacher.

What made you decide to blend mathematics and biology?

I chose to study molecular biology and mathematics at the University of Vienna. At the completion of my undergraduate degree, I began to investigate places where I could pursue both of those fields. Around this time, I was invited to a conference in Italy, where I met a number of researchers who were applying mathematics to cancer processes. They mentioned that Harvard was one place where such research was being pursued.

I was accepted into Harvard's doctoral program for evolutionary biology, a subspecialty of biology that examines the change of populations over time by variation and selection. It was there that I began to realize that I could apply mathematics to understanding the biology of cancer. I came to MSKCC in 2007 and continue to work in this interdisciplinary field.

How do you use mathematical models to predict how cancers behave?

The art of mathematical modeling is to choose the right level of abstraction. The goal is to look at a complex biological system and build a

mathematical framework to describe it. This framework should be as simple as possible, but not simplistic — it has to capture the essential characteristics of the system. The math we use can be quite simple. We want to be able to capture several aspects of a biological process, but not so many that the model becomes too complicated. Our goal is to take what we know and use the model to learn more about what we don't know.

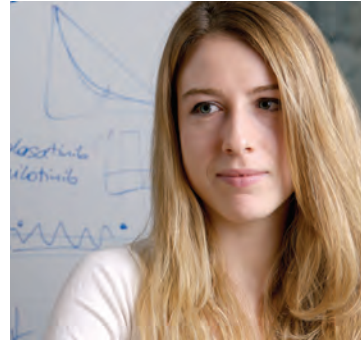
With regard to cancer, we take what we know about a disease, such as the type of mutations that drive a particular type of tumor, and construct a mathematical model describing the steps leading to an observed biological outcome. This outcome could be tumor initiation, disease recurrence, the development of resistance to therapy, or other processes. Then we try to validate the predictions of the model in cell lines or in mice. The mouse modeling experiments might involve introducing mutations at specific times and locations in the animal, or following a new dosing schedule for a treatment and seeing what happens.

If the animal experiment does not match the prediction we made using the model, then we use any information we obtain from the animal study to refine the model so it conforms to what is happening. It's an ongoing process of testing and reformulating.

How are you using mathematical models to study brain tumors?

I am collaborating with investigators from the Brain Tumor Center to identify the probable cell of origin for gliomas and the most likely order in which mutations arise to make the cell cancerous. We're also studying how cancer cells develop resistance to therapy, which is a significant challenge in the treatment of malignant brain tumors and the reason why many therapies eventually stop working.

Brain tumors such as glioblastomas lend themselves to this type of research, due to the pioneering work of Dr. Eric Holland and colleagues who developed a mouse model in which particular mutations can be induced in a very specific manner. These researchers are able to turn specific genes on and off at precise times and in defined cell types. That makes it easier to



test the predictions generated by our mathematical models and correlate those predictions with the outcomes we observe.

What is the PS-OC and how will it further your research?

The PS-OC at MSKCC is one of 12 such centers established with a grant

from the National Cancer Institute. It brings together experts from physics, mathematics, chemistry, engineering, and oncology to better understand the physical and biological principles of oncology. Our PS-OC is focused on the evolutionary dynamics of cancer. Cancer develops as a result of an evolutionary process in tissues, and the laws of evolution can be best formulated as mathematical equations. The PS-OC initiative is a great platform for combining math with clinically important questions to test models for cancer and explore new theories.

In addition, the PS-OC is enabling us to educate scientists at the beginning of their careers, as well as offer outreach programs to high school and university students considering a career in scientific research. I think it is very important to expose students to the idea that anything is possible — in our case, the combination of math, evolution, and medicine.

In what ways would you hope your research could improve the care of patients with cancer?

The possibility of having a real impact in the clinic is what gets me out of bed in the morning. I got into this because I think that a mathematical and computational approach has the potential to contribute to a better understanding of cancer, and eventually, to a better way of treating it. Right now we are working towards identifying more effective drugs for cancer patients, new ways of administering existing drugs, and novel approaches to targeting certain cell types or mutations. I never thought I'd end up being at a place like MSKCC, where there are so many colleagues and resources that help me blend mathematics and biology. There are a few places that do mathematical modeling, but it is the combination of math with the clinical data that we have here at MSKCC that gives us the opportunity to contribute to clinically important problems.

BTC RESEARCH GRANT RECIPIENTS

2007–2009: 20 BTC GRANTS AWARDED FOR A TOTAL OF \$2.1M

Funded by the F. M. Kirby Foundation

2009 GRANT WINNERS



Lindy Barrett, PhD

CANCER BIOLOGY & GENETICS

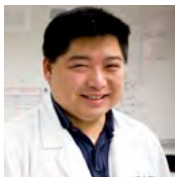
The Role of Id Proteins in Glioblastoma Multiforme (GBM) Tumorigenesis



Oren Becher, MD, Jason Huse, MD, PhD, Praveen Raju, MD, PhD

PEDIATRICS, PATHOLOGY, PEDIATRIC NEUROLOGY

Molecular Characterization and Stratification of Human Medulloblastomas



Timothy Chan, MD, PhD

RADIATION ONCOLOGY, HUMAN ONCOLOGY AND PATHOGENESIS PROGRAM

Understanding the Function of the Tyrosine Phosphatase PTPRD, a Frequently Inactivated and Mutated Tumor Suppressor in Glioblastoma



Jason Huse, MD, PhD

PATHOLOGY

Biomarker Development for the Molecular Subclassification of Malignant Glioma



Andrew Lassman, MD, Ingo Mellinghoff, MD

NEUROLOGY, NEUROLOGY/HUMAN ONCOLOGY AND PATHOGENESIS PROGRAM

Pulsatile Kinase Inhibitor Therapy for Malignant Glioma: Proof of Concept Clinical Trial



Tatsuya Ozawa, MD, PhD

CANCER BIOLOGY & GENETICS

The Discovery of the Genetic Events Cooperating with NF1 Inactivation in Gliomagenesis



Teodoro Pulvirenti, PhD

CELL BIOLOGY

Wnt Signaling in Gliomas and the Control of Stem-Like, Glioma Cell Fate

2008 GRANT WINNERS

Kathryn Beal, MD
Oren Becher, MD
Bipin Bhatia, PhD
Cameron Brennan, MD
Steven Foster, PhD
Ruimin Huang, PhD
Xinjiang Wang, PhD
Robert Young, MD

2007 GRANT WINNERS

Michelle Bradbury, MD, PhD
Luca Cartegni, PhD
Daniel Ciznadija, PhD
Adilia Hormigo, MD, PhD
Andrew Lassman, MD
Michael McDevitt, PhD

PHYSICIANS IN THE MEDIA



Dr. Philip Gutin in *Vital Signs*
with Dr. Sanjay Gupta
CNN, February 2009



Dr. Lisa DeAngelis on *World News*
with Charlie Gibson
ABC News, August 2009

MAJOR BENEFACTORS OF THE BRAIN TUMOR CENTER AND FACULTY

\$10,000,000

Simons Foundation

\$2,500,000 to \$9,999,999

F. M. Kirby Foundation

Bruce C. Ratner

Tow Foundation

\$1,000,000 to \$2,499,999

Abrams Trust

Charlotte and Bill Ford

Robert J. Kleberg, Jr., and Helen C. Kleberg Foundation

Leon Levy Foundation

Litwin Foundation

John and Michael Chandris

\$100,000 to \$999,999

Alex's Lemonade Stand

Brain Tumor Funder's Collaborative

Children's Brain Tumor Foundation

The Dana Foundation

Doris Duke Charitable Foundation

Genentech

Kids for Survival/Wasserman Family

Brain Tumor Society

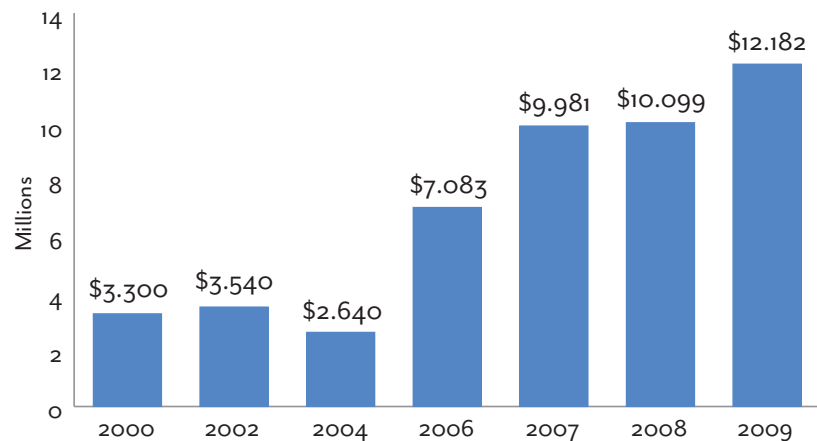
St. Baldrick's Foundation

Estate of Woodrow Q. Smith

Sontag Foundation

Kendrick R. Wilson III

SPENDABLE NIH DOLLARS RECEIVED WITH BTC MEMBER AS LEAD PI
BRAIN-RELATED NIH \$



2009 NEW NIH GRANTS (TOTAL \$ AWARD)



Alexandra Joyner, PI
\$2.37M

NATIONAL INSTITUTE OF MENTAL HEALTH
R01: Engrailed Genes and Cerebellum Morphology, Spatial Gene Expression and Circuitry



Eric Holland, PI
\$6.62M

NATIONAL CANCER INSTITUTE
U01: P3IK Signaling and Biology of Therapeutic Response in Brain and Prostate Tumors

R01: Requirements for Generation and Maintenance of Gliomas



Lorenz Studer, PI
\$1.03M

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
R01: Defining Fate Potential in Human ESC Derived Neural Stem Cells



Michelle Bradbury, PI
\$835K

NATIONAL CANCER INSTITUTE
R21: MRI-PET Guided Stereotactic Biopsy of High Grade Gliomas



Franziska Michor, PI
\$11M

NATIONAL CANCER INSTITUTE
U54: Physical Sciences – Oncology Center (PSOC) Evolutionary Dynamics of Brain, Lung, and Hematopoietic Tumors

PUBLICATIONS & COLLABORATIONS

BTC leadership actively promotes interactions that lead to jointly authored publications. The table below illustrates that publications and collaborations have more than doubled in recent years. This progressive increase in brain tumor-related publications demonstrates the impact of the expansion of the neuro-oncology program at MSKCC and recruitment of dedicated physician-scientists with an interest in brain tumors. In just 2009, the BTC members have also collaborated with 16 countries across the globe in brain-related topics. The BTC has recognized the need for organized efforts and collaborations and continuously works towards further fostering new interactions.

2009 COLLABORATIONS ACROSS THE GLOBE



MSKCC PUBLICATIONS IN BRAIN-TUMOR-RELATED TOPICS

Including joint publications (■), by Year (n=596)



2009-2010 LEON LEVY YOUNG INVESTIGATORS

Funded by the Leon Levy Foundation



Dolores Hambarzumyan, PhD
Department of Neurosurgery



Jason Huse, MD, PhD
Department of Pathology



Franziska Michor, PhD
Computational Biology Program

2009 PUBLICATIONS

In 2009, the BTC members published a total of 93 articles in 55 journals.

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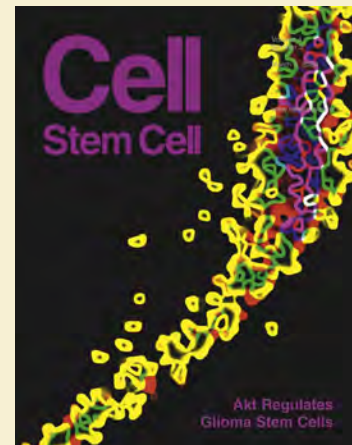
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2009-2010 JOURNAL COVERS FROM BTC ARTICLES



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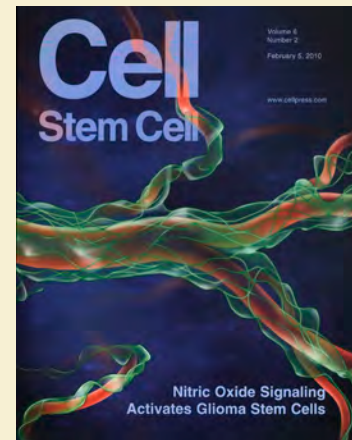
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MESSAGE FROM THE DIRECTOR

The expertise and experience of Memorial Sloan-Kettering's Brain Tumor Center (BTC) ensures that when patients come here for treatment, they receive the absolute best care available today from the same physicians and scientists leading our way to the medical breakthroughs of tomorrow. As we unite surgeons, oncologists, and radiation oncologists with molecular biologists, physicists, engineers, and computational biologists, the Brain Tumor Center is dedicated in all its efforts to developing more effective treatments and setting new therapeutic standards.

In 2009 and 2010, many of the Brain Tumor Center's achievements in the laboratory saw direct translation into the clinic. Our researchers have defined molecular signal transduction subclasses of malignant gliomas, which will allow rational use of novel small molecule inhibitors in clinical trials. In addition, several of our laboratories have begun to unravel the role of glioma stem cells in resistance to therapy and tumor recurrence. Better animal models, genetically engineered to more accurately mimic human tumors, have dramatically improved our understanding of brain tumor biology and led to clinical trials in adults and children. Critically, we are getting

closer to the goal of molecularly characterizing each patient's tumor and providing individually tailored therapies and clinical trials.

Since its founding in 2007, the Brain Tumor Center has been a driving force behind a substantial increase in high-profile publications, NIH grant support, and clinical trials. Thanks to the generosity of our philanthropic partners and the hard work of our administrative staff, the BTC's internal peer-reviewed grant series now funds six projects led by early-career investigators in the field of clinical and basic brain tumor research each year. The BTC seminar series continues to attract international leaders in brain tumor research. Finally, our faculty retreat held this spring was given outstanding marks by our external advisory board.

The Brain Tumor Center has already achieved remarkable success over its lifetime and continues to redefine the treatment standards and outcomes for patients with these tumors. I am delighted to present this 18-month report documenting our efforts.

Eric Holland, MD, PhD

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Cancer Center

Brain Tumor Center
1275 York Avenue, Box 71
New York, NY 10065
Telephone: 212-639-6661
E-mail: btc@mskcc.org
www.mskcc.org/brain tumors