

PROGRESS

VISION

TRANSLATIONAL

RESEARCH

DEVELOP

THERAPY

TRAINING

COMMITMENT

INSIGHT

TREATMENT

INNOVATION

INVESTIGATE

COLLABORATION

ACCELERATE

STRATEGY

SCIENCE

TECHNOLOGY

LABORATORY

ADMINISTRATION

DISEASE

MECHANISMS

GENETICS

PREVENTION

COMMUNITY

ONCOGENESIS

FOCUS



MEMORIAL SLOAN-KETTERING CANCER CENTER

The Human Oncology and Pathogenesis Program

2006–2010 Progress Report

The Human Oncology and Pathogenesis Program (HOPP) has a goal to be progressive in various areas of cancer research. From its inception in 2006 through 2010, HOPP achieved significant progress in training, collaboration, and innovation to ensure its impact on the Center and its patients.



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In conjunction with the Center's effort to be more environmentally conscious, this report can also be accessed at [www.mskcc.org/hopp](http://www.mskcc.org/hopp).



The Human Oncology and Pathogenesis Program was established at MSKCC in 2006 to accelerate the development and implementation of novel experimental therapeutic strategies in cancer. This coincided with the initiation of large-scale human tumor resequencing projects by the National Cancer Institute and others (including HOPP investigators) that have led to a wealth of cancer genomics data that was inconceivable just five years ago. Consequently, cancer care is undergoing a dramatic “molecular” transformation. This has already led to diagnostic tests that can dramatically increase the probability that a patient will respond to treatment and to the discovery of more effective, less toxic drugs that specifically target molecular lesions in tumors.

Since its inauguration five years ago, HOPP has grown from a founding group of five principal investigators to fifteen full time faculty who employ over 200 postdoctoral fellows, medical fellows, graduate students, and research staff. HOPP laboratories currently occupy nearly three floors in the Zuckerman Research Center with additional recruitment ongoing.

Research in HOPP spans a broad spectrum of cancer types, including breast cancer, colon cancer, glioblastoma, melanoma, leukemia, lung cancer, prostate cancer, sarcoma, and thyroid cancer. HOPP faculty come from diverse clinical training backgrounds, including endocrinology, medical oncology, neurology, neurosurgery, pathology, and radiation oncology. Consequently, the clinical impact of research conducted by HOPP investigators is broad and, in a very short time, has resulted in internationally recognized advances in the treatment of lung cancer, melanoma, prostate, and thyroid cancers.

A founding principle of HOPP is that all faculty members are clinically trained physician-scientists. While HOPP faculty spend most of their time conducting laboratory research, all are also embedded in clinical or disease management teams relevant to their laboratory work. This interaction with full-time clinical colleagues enables efficient communication of new laboratory insights into clinical trials as well as early recognition of new clinical observations that merit more intensive laboratory investigation. These two-way interactions, lab-clinic and clinic-lab, are essential to successful translational research.

As the inaugural chair of HOPP, I am thrilled with the progress made by my colleagues over these first five years. While it is fine to pause briefly and acknowledge our success, we cannot rest on our laurels. There is much more we can do in the fight against cancer. With the constantly expanding insights into the molecular causes of cancer and the ever-improving technologies to elucidate these causes in our patients, the timing could not be better for us to make even more dramatic progress in our quest to end the suffering from this dreaded disease.

A handwritten signature in black ink that reads "Charles L. Sawyers".

Charles L. Sawyers, MD  
Investigator, Howard Hughes Medical Institute  
Chair, Human Oncology and Pathogenesis Program  
Memorial Sloan-Kettering Cancer Center

- ▶ Dr. Sawyers earned his undergraduate degree from Princeton University and his MD degree from Johns Hopkins School of Medicine.
- ▶ Dr. Sawyers became the Chair of HOPP in 2006 and a Howard Hughes Medical Institute (HHMI) investigator in 2008.
- ▶ In 2009, Dr. Sawyers received the Lasker~DeBaakey Clinical Medical Research Award.
- ▶ Go to [Wikipedia.org](http://Wikipedia.org) to learn more about HOPP and Dr. Sawyers.

The Human Oncology and Pathogenesis Program (HOPP) was created in 2006 under the leadership of Dr. Charles Sawyers. Listed below is an overview of the Clinical Departments represented in HOPP as well as information on HOPP faculty and the Administrative Team.

### CLINICAL DEPARTMENTS REPRESENTED IN HOPP

Department of Medicine  
Leukemia Service  
Endocrinology Service  
Genitourinary Oncology Service

Department of Pathology  
Department of Neurosurgery

Department of Neurology  
Department of Radiation Oncology

### 2010 FACULTY & ADMINISTRATION

#### FACULTY (14)

[Charles Sawyers, MD](#)  
*HOPP Chair, Member*  
*Leukemia Service, Department of Medicine*

[Boris Bastian, MD](#)  
*Member*  
*Chair, Department of Pathology*

[Cameron Brennan, MD](#)  
*Assistant Member*  
*Department of Neurosurgery*

[Timothy Chan, MD, PhD](#)  
*Assistant Member*  
*Department of Radiation Oncology*

[Emily Cheng, MD, PhD](#)  
*Associate Member*  
*Department of Pathology*

[James Fagin, MD](#)  
*Member*  
*Chief, Endocrinology Service, Department of Medicine*

[Adriana Heguy, PhD](#)  
*Associate Lab Member*

[James Hsieh, MD, PhD](#)  
*Associate Member*  
*Genitourinary Service, Department of Medicine*

[Jason Huse, MD, PhD](#)  
*Affiliate Member*  
*Department of Pathology*

[Marc Ladanyi, MD](#)  
*Member*  
*Department of Pathology*

[Ross Levine, MD](#)  
*Assistant Member*  
*Leukemia Service, Department of Medicine*

[Ingo Mellinghoff, MD](#)  
*Assistant Member*  
*Department of Neurology*

[Christopher Park, MD, PhD](#)  
*Assistant Member*  
*Department of Pathology*

[David Solit, MD](#)  
*Assistant Member*  
*Genitourinary Service, Department of Medicine*

#### ADMINISTRATION (13)

Ederlinda Paraiso  
*Administrator*

Cherryl Murray-Marone  
*Administrative Assistant*

Jenna Marie Dix  
*Administrative Assistant*

Emily Delgado  
*Administrative Assistant*

Ben Martin  
*Executive Assistant*

Matthew Skernolis  
*Fund Coordinator*

Erika Bernardino  
*Program Coordinator*

Lorraine Pistorino  
*Program/Fund Coordinator*

Vanessa Christopher  
*Research Secretary*

Barbara Cruz  
*Research Secretary*

Joseph Pablo  
*Research Secretary*

Christie Park  
*Research Secretary*

Camille Teta  
*Research Secretary*



## NUMBER OF TRAINEES/STAFF BY POSITION (2007–2010)

|                              | 2007      | 2008      | 2009       | 2010       |
|------------------------------|-----------|-----------|------------|------------|
| Clinical Attendings          | 8         | 10        | 11         | 13         |
| Research Fellows             | 24        | 34        | 45         | 66         |
| Clinical Fellows             | 4         | 6         | 9          | 17         |
| Visiting Investigators       | 3         | 4         | 4          | 7          |
| Graduate Students            | 6         | 6         | 8          | 16         |
| Research Technicians         | 16        | 23        | 31         | 48         |
| Summer Students / Volunteers | 0         | 3         | 15         | 40         |
| <b>Total:</b>                | <b>61</b> | <b>86</b> | <b>123</b> | <b>207</b> |



Omar Abdel-Wahab (left), Instructor, and Jay Patel, Research Technician, of the Levine Lab

## HOPP PHILANTHROPIC DONATIONS THROUGH 2010

### HOPP BENEFACTORS THROUGH 2010

#### \$10,000,000 - \$15,000,000

Tow Foundation  
Wallace Foundation

#### \$1,000,000 - \$5,000,000

Arnold Goldstein  
Jamie and Jeffrey Harris Family Foundation  
Trust of Henry H. Shepard

#### \$500,000 - \$999,999

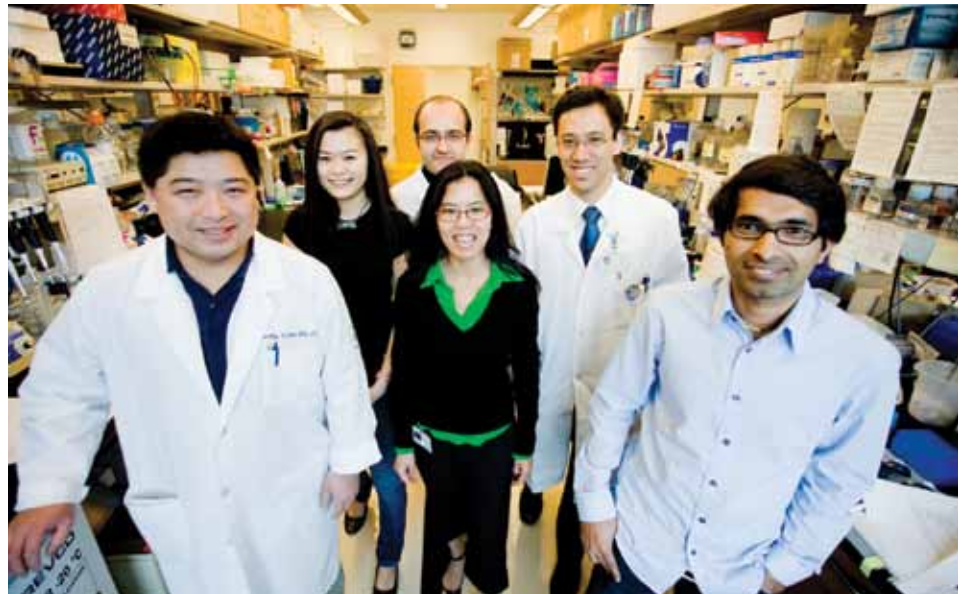
Mr. & Mrs. Stephen Anbinder  
Estate of Marion Carstairs

#### \$300,000 - \$499,999

Estate of Judith Helfant  
Myra and Edna Curl Research Foundation  
Society of Memorial Sloan-Kettering  
Cancer Center

#### \$75,000 - \$299,999

Frey Family Foundation  
Mr. & Mrs. Robert D. Allen  
William Randolph Hearst Foundations



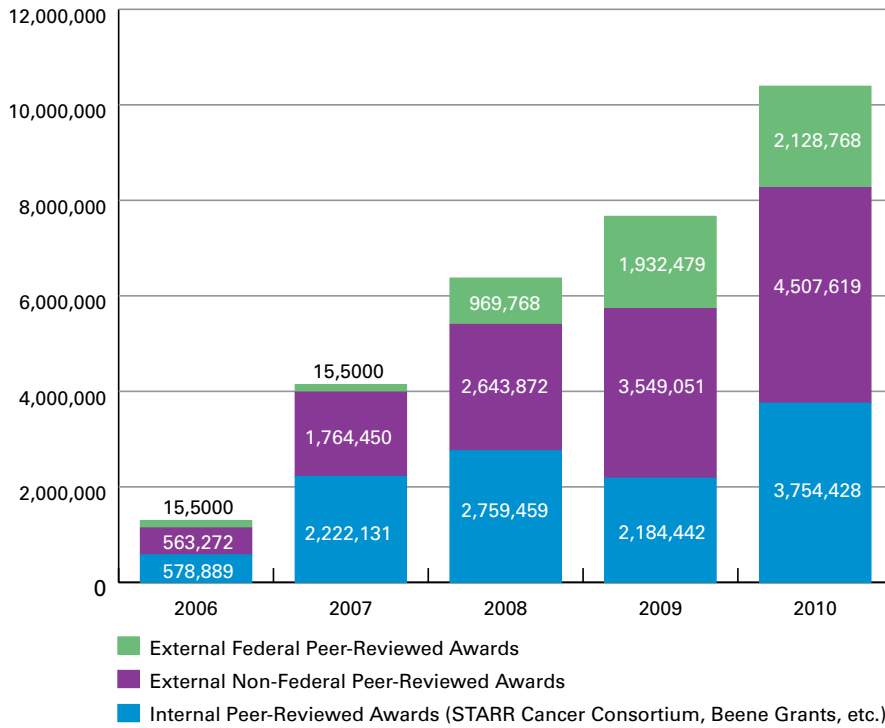
The Chan lab (from left): Timothy Chan, Shasha Meng, Fang Fang, Emrullah Yilmaz, Andreas Rimner, and Veeriah Selvaraju



Igor Vivanco, Research Associate, Mellinshoff Lab

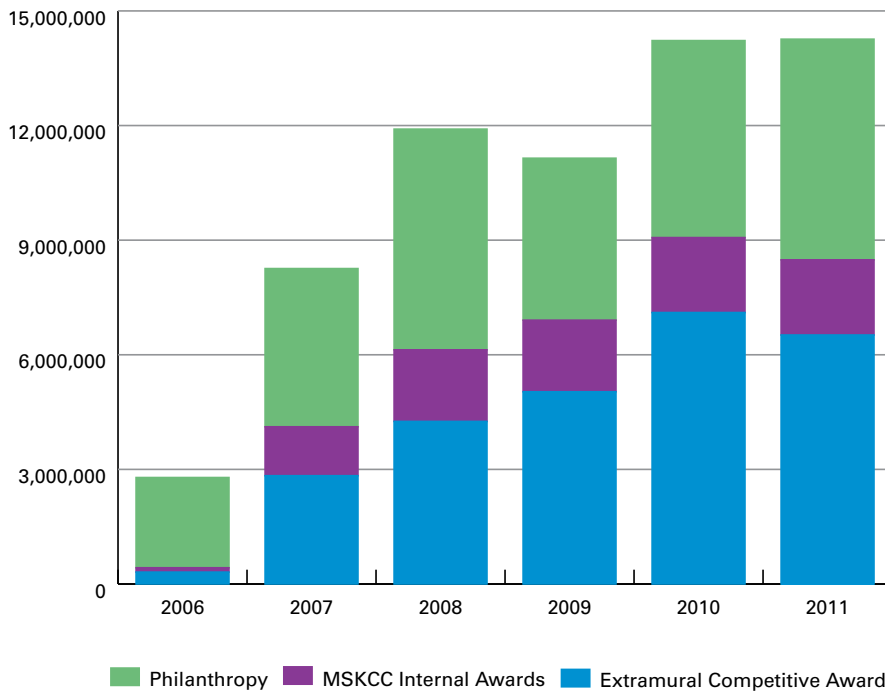
## FINANCIAL METRICS

**Competitive Peer-Reviewed Annual Awards Issued to HOPP Faculty & Trainees by Source of Funding (Direct Cost Only)**



The chart shows the increase in awards granted from 2006 to 2010. HOPP faculty have been very successful in earning outside support for their research endeavors throughout the years.

**Cost of HOPP Research  
Annual Expenses and Sources of Funding**



The chart shows total expenses for HOPP faculty from 2006 to 2011. Total expenses have risen over time in each of the three categories of external competitive awards, internal competitive awards and philanthropic donations.

HOPP's mission is to enhance translational cancer research at MSKCC by

1. Recruiting outstanding laboratory-based physician-scientists across clinical disciplines engaged in disease-focused research
2. Facilitating the creation of core infrastructure to enable state-of-the-art translational research activities
3. Providing a unique translational training environment for young physician-scientists and PhD laboratory scientists

### MECHANISMS AND DISEASES STUDIED

[colon cancer](#)  
[glioblastoma](#)

[leukemia](#)  
[lung cancer](#)

[melanoma](#)  
[prostate cancer](#)

[sarcoma](#)  
[thyroid cancer](#)

### SPOTLIGHT ON DR. DAVID SOLIT & THE GEOFFREY BEENE CANCER RESEARCH CENTER

#### PROGRESSIVE RESEARCH

“You need to understand the basis of the disease if you want to come up with a rational strategy to treat it.”

— Dr. David Solit

*Dr. David Solit has been a member of HOPP since 2006. His lab focuses on studying a variety of cancers. As a result, he understands the importance of being able to obtain the financial support needed to push new and innovative ideas forward.*

Philanthropic gifts allow major discoveries to be made. Key discoveries and advancements from philanthropic gifts let you try something that has never been tried before in order to generate preliminary data which later leads to NIH funding. This is all very true for my whole BRAF story. The original funding for all of our work with BRAF led to a drug that now has shown a survival benefit for patients with the BRAF mutant melanoma. The first seven years of my work was all funded through philanthropic funds, gifts to Memorial

Sloan-Kettering. It's money that allows us to explore some risky areas that can bring some major leaps in our knowledge. For example, I received seed funding to genetically characterize tumors in colon cancer. This helped us to discover new targets that we could potentially use as the basis for treating cancer. The reason that this is so important is that you need to understand the basis of the disease if you want to come up with a rational strategy to treat it. Now that we've identified these targets, we are applying for other funding to follow up on these discoveries. Needless to say, it can be very difficult to move in a new direction without philanthropic funding.



Drs. [David Solit](#), Assistant Member, HOPP, and Efsavia Vakiani, Assistant Attending, Department of Pathology

HOPP works with the Geoffrey Beene Cancer Research Center and Foundation in many other ways. To learn more, visit [www.mskcc.org/beene](http://www.mskcc.org/beene).

Clinical expertise and research focus areas are what propel progressive translational cancer research within HOPP. There are fourteen laboratories in HOPP. Each capitalizes on new opportunities to further translational research at the Center.

Learn more about our faculty and the unique work being done in their labs.



**CHARLES SAWYERS, MD**

Chair, Faculty

#### LAB MEMBERS

Vivek Arora

*Clinical Research Fellow*

Minna Balbas

*Graduate Research Assistant – GSK*

Trever Bivona

*Clinical Research Fellow*

Ling Cai

*Research Scholar*

Brett Carver

*Assistant Attending*

Caren Chapinski

*Research Technician*

Yu Chen

*Special Fellow*

Daniel Danila

*Instructor*

Michael Evans

*Clinical Research Fellow*

Haley Hieronymus

*Senior Research Scientist*

Phillip Iaquina

*Research Fellow*

Philicia Moonsamy

*Research Technician*

William Polkinghorn

*Clinical Research Fellow*

Tambudzai Shamu

*Research Technician*

Mingliang Wan

*Research Technician*

Philip Watson

*Research Associate*

Douglas Wheeler

*Graduate Research Assistant – MD/PhD, WCMC*

John Wongvipat

*Lab Manager*

Fiona Yinan Chen

*Graduate Research Assistant – UCLA*

#### SPOTLIGHT ON GASTROINTESTINAL STROMAL TUMORS

##### **Yu Chen, MD, Special Fellow, Department of Medicine**

Dr. Yu Chen is a Medical Oncology Fellow in the Department of Medicine as well as a Postdoctoral Fellow in the Sawyers lab. His work focuses on gastrointestinal stromal tumor, or GIST, which is one of the most common types of human sarcomas. GIST has been notoriously resistant to conventional treatment, such as chemotherapy. In 1998, a seminal discovery showed that GIST was caused by a mutation in the growth factor receptor KIT. Since then, the KIT inhibitor imatinib (Gleevec) has become the mainstay of GIST treatment, inducing temporary responses in the majority of patients.

While working in the Sawyers lab, Dr. Chen discovered a second oncogene, ETV1, that is required for GIST tumors. ETV1 is very highly expressed in GIST. Targeting ETV1 expression through “knockdown” technology inhibits growth of GIST cells in culture and in mouse models. Their mechanistic studies showed that KIT mutations cause the oncogenic ETV1 protein to accumulate in cells. Currently, Dr. Chen is investigating ways to target ETV1 to inhibit either its accumulation or its function.

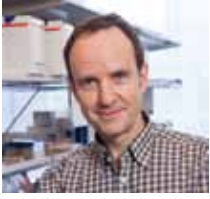
#### RESEARCH FOCUS

The Sawyers laboratory is focused on characterizing signal transduction pathway abnormalities in various cancers, including chronic myeloid leukemia and prostate cancer, with an eye toward translational implications. Dr. Sawyers’ research is best demonstrated through his studies of BCR-ABL tyrosine kinase function in chronic myeloid leukemia, his work with Brian Druker and Novartis in the development of imatinib as primary therapy for CML, and his discovery that imatinib resistance is caused by BCR-ABL kinase domain mutations.

This discovery led Dr. Sawyers to evaluate second-line Abl kinase inhibitors, such as the dual Src/Abl inhibitor dasatinib, which received fast-track approval from the FDA in June 2006.

Dr. Sawyers has also developed a leading laboratory-based program in prostate cancer. This work is currently focused on the role of the androgen receptor in disease progression, even when tumors progress to the hormone-refractory stage. After demonstrating that higher levels of androgen receptor are necessary and sufficient to confer resistance to current antiandrogens, Dr. Sawyers collaborated with UCLA chemist Michael Jung to discover a small molecule inhibitor that targets the increased levels of androgen receptor found in hormone refractory disease by a novel mechanism. A phase I–II trial of this compound (MDV3100), completed at MSKCC and other sites, showed impressive clinical responses in men with castrate-resistant prostate cancer, including those who have progressed on chemotherapy. A phase III trial is underway.





## BORIS BASTIAN, MD, PhD

Faculty

### LAB MEMBERS

Thomas Botton  
*Research Fellow*

Nancy Bouvier  
*Lab Manager*

Maria Garrido  
*Research Fellow*

Klaus Griewank  
*Research Fellow*

Shea Loy  
*Research Technician*

Rajmohan Murali  
*Research Associate*

Andrea Saggini  
*Research Fellow*

Mustafa Mert Sozen  
*Research Fellow*

Alyssa Sparatta  
*Research Technician*

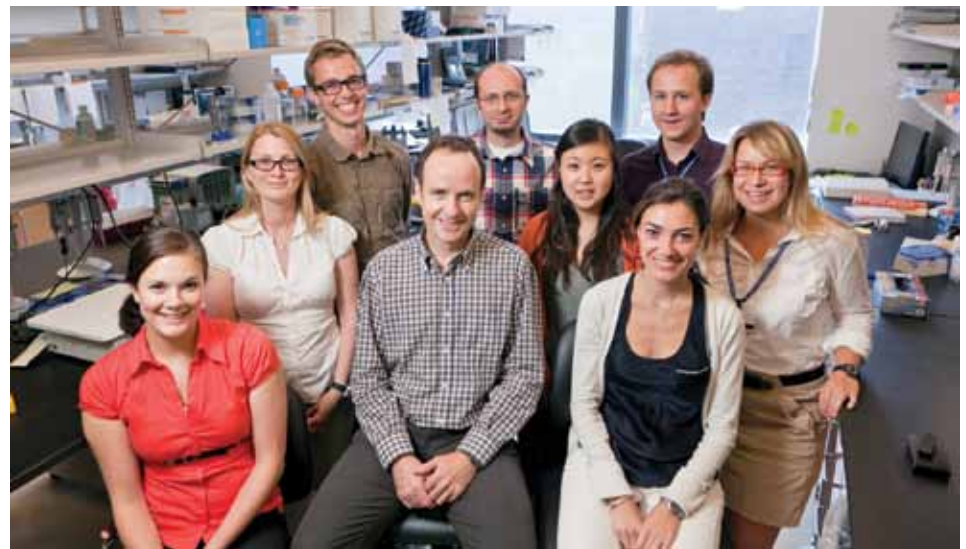
Tomas Wiesner  
*Research Fellow*

### SPOTLIGHT ON UVEAL MELANOMA

#### Klaus Griewank, MD, Research Fellow

Dr. Klaus Griewank spent four years doing basic research in immunology, two of which were at the University of Chicago with Professor Albert Bendelac.

After experiencing firsthand the limited therapeutic options available for melanoma treatment in the clinic, Dr. Griewank decided to take a sabbatical to pursue research in Boris Bastian's lab on malignant melanoma. In the Bastian lab, Dr. Griewank is focusing on understanding the signaling downstream of the newly identified uveal melanoma oncogenes GNAQ and GNA11. The lab is working on setting up inducible mouse models in the hope that a better understanding of the mechanisms involved will allow the development and evaluation of targeted therapies.



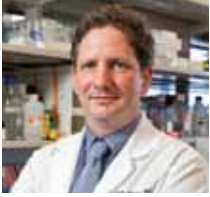
The Bastian Lab (from right): Maria Garrido, Alyssa Sparatta, Thomas Weisner, Christie Park, Mustafa Mert Sozen, , Boris Bastian, Thomas Botton, Nancy Bouvier, and Shea Loy

### RESEARCH FOCUS

The Bastian laboratory's research interest is focused on the molecular genetics of melanoma with a particular focus on the discovery of genetic alterations useful for diagnosis, classification, and therapy.

Using genome-wide DNA copy and mutation analyses and by correlating them with clinical and histomorphologic features, the Bastian lab has identified distinct subtypes of melanoma.

These findings have become clinically relevant, as the subtypes are enriched in specific mutations, such as in KIT and BRAF, for which specific inhibitors are already approved or under advanced clinical investigation. Dr. Bastian believes that an improved disease classification with the precise delineation of biologically distinct, molecularly defined subtypes is the key to improving prevention, diagnosis, and therapy of melanoma.



## CAMERON BRENNAN, MD

Faculty

### LAB MEMBERS

Debyani Chakravarty  
*Research Associate*

Alicia Pedraza  
*Senior Research Assistant*

Nicholas Szerlip  
*Surgical Research Fellow*

### SPOTLIGHT ON GLIOBLASTOMA MULTIFORME

#### Nicholas Szerlip, MD, Surgical Research Fellow

Dr. Nicholas Szerlip was trained in neurosurgical oncology at the NIH and Memorial Sloan-Kettering. He is continuing his research endeavors by examining glioblastoma multiforme (GBM), which is an aggressive primary brain tumor clinically resistant to therapy. One reason for the poor clinical response lies in the heterogeneity of this tumor.

The Brennan lab's research takes the perspective that this tumor is a community of cells and like any community is made up of a heterogeneous mix. These different subpopulations affect core cancer pathways in different ways and respond differently to chemotherapeutic agents. Dr. Szerlip's research has begun to identify molecular signatures that define these different subpopulations.

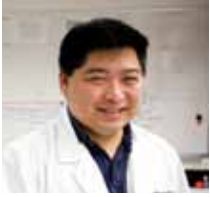
This multifaceted approach explores how these different subpopulations interact and how they respond to targeted treatment in the context of the cellular community. The lab hopes this can lead to better treatment paradigms and better clinical responses.

### RESEARCH FOCUS

Dr. Brennan's research is directed at the characterization of genetic alterations and patterns of signal transduction pathway dysregulation in brain tumors. He has developed novel computational approaches for integrated genomic analysis, leading to the discovery of p18 as a tumor suppressor and target of deletion in glioma, the identification of the first functional fusion gene in a glioblastoma tumor (KDR-PDGFR $\alpha$  fusion), and the characterization of new molecularly defined subclasses of glioblastoma.

Dr. Brennan has been a leading contributor within The Cancer Genome Atlas pilot project in glioblastoma.





## TIMOTHY CHAN, MD, PhD

Faculty

### LAB MEMBERS

Victoria Banuchi  
*Surgical Research Fellow*

Stephanie Eng  
*Research Technician*

Armida Mathilde Fabius  
*Research Fellow*

Fang Fang  
*Research Fellow*

Ian Ganly  
*Assistant Attending*

Anuj Goenka  
*Clinical Research Fellow*

Yongxing Gong  
*Research Fellow*

Andrew Kaufman  
*Research Technician*

Luc Morris  
*Surgical Research Fellow*

Berenice Ortiz  
*Graduate Research Assistant – GSK*

Andreas Rimmer  
*Clinical Research Fellow*

David Roy  
*Medical Student*

Sevin Turcan  
*Research Fellow*

### SPOTLIGHT ON ORAL CANCER

#### Luc Morris, MD, Surgical Research Fellow

Dr. Luc Morris is a Head and Neck Surgery Fellow at MSKCC, with a research interest in oral cancer. He has been working on understanding genetic alterations in a common cancer signaling pathway, the PI3 kinase pathway, in oral cancers. This is a commonly altered pathway in many types of cancer that can be targeted with promising new drugs currently in clinical trials.

The Chan lab has identified several genetic alterations that they believe lead to this pathway becoming activated, helping us to better target clinical trials of new drugs for oral cancer. As part of their research, they used a next-generation technology located at MSKCC that allowed them to simultaneously study gene copy numbers at 1 million locations across the genome. This data allowed the lab to identify two previously unknown genes that seem to significantly contribute to the genetic basis of brain, colon, and head and neck cancers, which have formed the basis of ongoing work in the Chan lab.

These results, which Dr. Morris presented at two international cancer meetings this year, have relied on collaborations with several different labs in HOPP, and across MSKCC, exemplify the incredible resources available here to junior investigators.

### RESEARCH FOCUS

Dr. Chan's research focuses on elucidating the genomic changes that underlie oncogenesis. The lab is interested in understanding the genetic and epigenetic changes that give rise to glioblastoma, colon cancer, and breast cancer.

Specifically, they utilize genomic strategies to identify and characterize tumor suppressor genes that are broadly inactivated in human cancers. Examples of tumor suppressors identified by the Chan lab include PTPRD and PARK2.

The Chan lab has recently shown that the PTPRD tyrosine phosphatase is a tumor suppressor that is inactivated in a number of human cancers. The PTPRD locus undergoes copy number loss, mutation, and/or epigenetic silencing in a large fraction of tumors. The Chan group showed that the PTPRD gene, which is on 9p23, helps drive chromosome 9p loss in cancer.

Furthermore, they identified STAT3 as a functional target of PTPRD. They have also recently identified a familial Parkinson's disease gene, PARK2, as a multisite tumor suppressor on chromosome 6q25-27, another region frequently lost in cancer. The Chan lab found that PARK2 is mutated in human malignancies and that these mutations inactivate the E3 ligase activity of the protein product. PARK2 inactivation leads to cyclin E dysregulation and mitotic instability. These observations are the first definitive data that provide a direct link between the neurodegenerative condition Parkinson's disease and cancer.

Current efforts in the lab focus on characterizing the mechanisms of action of these two tumor suppressor genes and developing animal models to determine the roles of these genes in oncogenesis.



## EMILY CHENG, MD, PhD

Faculty

### LAB MEMBERS

Gregory Bean  
*Graduate Research Assistant  
Medical Scientist Training Program (MSTP)*

Po Chan  
*Research Technician*

Yafen Huang  
*Research Fellow*

Chung Ping Liao  
*Research Fellow*

Ho Chou Tu  
*Research Fellow*

Gary Wang  
*Graduate Research Assistant  
Medical Scientist Training Program (MSTP)*

Kouhei Yamamoto  
*Visiting Investigator*

Chunjun Zhao  
*Research Technician*

### SPOTLIGHT ON PROGRAMMED CELL DEATH

#### Ho-Chou Tu, PhD, Research Fellow

Dr. Ho-Chou Tu joined Dr. Emily Cheng's laboratory in 2005 to conduct her PhD thesis on programmed cell death. Now, as a research fellow, she focuses on BAX/BAK-dependent apoptotic and BAX/BAK-independent necrotic programs. Her studies on apoptosis demonstrated that BID, BIM, and PUMA are essential for activation of the BAX- and BAK-dependent apoptosis, and her works on necrosis discovered a p53-cathepsin axis that cooperates with ROS to activate programmed necrotic death upon DNA damage.

Dr. Ho-Chou Tu received her doctoral degree in July 2010 with first-authored papers in *PNAS* and *Science*. She hopes to translate knowledge obtained from studying cell death mechanisms to the development of novel anticancer therapeutic strategies.

### RESEARCH FOCUS

Dr. Cheng's research focuses on investigating the molecular mechanisms underlying cell death with the hope that the knowledge derived from her research can be translated into targeted therapeutics that trigger cell death in cancer.

Her prior studies have helped delineate the mammalian core apoptotic pathway governed by the BCL-2 family proteins at the mitochondrion. The BH3-only molecules activate multidomain pro-apoptotic BAX and BAK to trigger a mitochondrion-dependent cell death program, which releases cytochrome c to activate caspases and initiates caspase-independent mitochondrial dysfunction. On the contrary, anti-apoptotic BCL-2 family proteins, including BCL-2, BCL-XL, and MCL-1, inhibit apoptosis by sequestering BH3-only molecules, thus preventing the activation of BAX/BAK.



Gregory Bean, Graduate Research Assistant

Dr. Cheng's recent work (1) subdivides the BH3-only molecules into BAX/BAK "activator" or BCL-2/BCL-XL/MCL-1 "inactivator" subgroups and establishes a hierarchical regulatory schema to integrate the interplay among various BCL-2 subfamilies; (2) defines a p53-cathepsin axis in DNA damage-induced programmed necrotic death; (3) discovers a VDAC2-BAK rheostat in controlling thymocyte survival and negative selection; and (4) proposes a stepwise activation model of BAX and BAK driven by BID, BIM, and PUMA in the initiation of mitochondrial apoptosis.

Dr. Cheng's ongoing research seeks to delineate three major cell death pathways: (1) BAX/BAK-controlled mitochondrial apoptotic programming, (2) BAX/BAK-dependent caspase-independent mitochondrial dysfunction, and (3) BAX/BAK-independent cell death. Moreover, Dr. Cheng's laboratory will explore whether and how deregulation of these cell death pathways contributes to the pathogenesis and treatment response of human cancer.





## JAMES FAGIN, MD

Faculty

### LAB MEMBERS

Xu Chen  
*Research Fellow*

Jose Miguel Dominguez  
*Research Fellow*

Aime Franco  
*Research Scholar*

Matti Gild  
*Research Fellow*

Jeffrey Knauf  
*Associate Attending*

Cristina Montero-Conde  
*Research Fellow*

Gisele Oler  
*Research Fellow*

Julio Ricarte Filho  
*Research Fellow*

Sergio Ruiz-Llorente  
*Research Fellow*

Mabel Ryder  
*Assistant Attending*

Sushil Vundavalli  
*Research Technician*

### SPOTLIGHT ON NF2

#### Julio Ricarte Filho, PhD, Research Fellow

Dr. Julio Ricarte Filho is a Research Fellow working with the Fagin lab at MSKCC. His work is focused on identifying genetic and genomic alterations of poorly differentiated and anaplastic thyroid cancers.

Currently, one of his projects involves the characterization of NF2 (neurofibromatosis 2) tumor suppressor in thyroid tumorigenesis. Although NF2 gene alterations have been primarily found within a restricted group of tumors (schwannomas, meningiomas, and mesotheliomas), Dr. Ricarte Filho recently found that this gene is lost in a subset of advanced thyroid cancers by different mechanisms, such as allelic loss, mutation, and posttranscriptional modifications. Re-expression of this protein in NF2-null cells strongly inhibits cell growth, at least in part by its suppressive effects on the MAPK pathway, through mechanisms he is now exploring.

Dr. Ricarte Filho is also investigating the phenotype and molecular alterations of thyroid glands in mice with targeted NF2 inactivation.

### RESEARCH FOCUS

The focus of Dr. Fagin's work is to understand the pathogenesis and the biology of thyroid cancers, with the goal of identifying new molecular-based therapies.

Thyroid cancer is the most common endocrine malignancy. Exposure to radiation during childhood confers increased predisposition to this disease. Dr. Fagin's lab has been instrumental in characterizing many of the somatic genetic changes associated with thyroid tumor initiation and progression in both radiation-induced and sporadic thyroid cancer, and in defining the functional consequences using in vitro and in vivo experimental models. He has focused in particular on the role of MAP kinase effectors, because these tumors are associated with a high prevalence of non-overlapping activating mutations of at least six genes encoding effectors in the pathway: the tyrosine kinase receptors RET and NTRK, the three RAS genes, and BRAF.

Dr. Fagin's present efforts are in the following areas:

- ▶ Development and refinement of animal models of thyroid cancer to further probe the signaling pathways required for transformation
- ▶ Identification of determinants of sensitivity/resistance to selective RAF and MEK inhibitors in thyroid cancer
- ▶ Exploration of the mechanisms by which innate immune cells in the microenvironment of thyroid cancers contribute to the development of the disease





## ADRIANA HEGUY, PhD

Faculty

### LAB MEMBERS

Olga Aminova  
*Senior Research Technician*

Igor Dolgalev  
*Bioinformatician Technician*

Kety Huberman  
*Senior Research Assistant*

Andrew Kayserian  
*Research Technician*

Demitri Lifgren  
*Volunteer*

Armory Meltzer  
*Volunteer*

Sabrena Thomas  
*Research Technician*

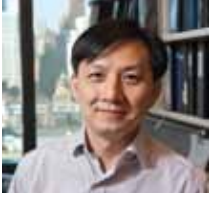
### THE GEOFFREY BEENE TRANSLATIONAL CORE

The Geoffrey Beene Translational Core is managed by Dr. Adriana Heguy. Dr. Heguy joined HOPP in 2007 and has been managing the core since its inception. The core processes and characterizes molecularly mostly human samples, from clinical and preclinical studies. The core performs mutation and single-nucleotide polymorphism detection, gene expression and DNA methylation analyses, and related assays of interest for translational oncology. The services the Beene Core provides are listed below:

- ▶ Semi-automated high-throughput nucleic acid (DNA and RNA) extraction and quality control from both archived and newly acquired clinical specimens, including frozen tissue, formalin-fixed paraffin-embedded (FFPE) samples, blood, cytopsins, etc. The Core also archives the DNA and maintains a DNA database of all material that it processes.
- ▶ Whole-genome amplification (WGA) of DNA extracted from these samples.
- ▶ Fully automated high-throughput PCR in 384 well plates, to provide templates for exon re-sequencing (Sanger or next-generation sequencing (454 or SOLiD – with Genomics Core Lab).
- ▶ Automated mutation detection and data analysis using software applications designed by the Bioinformatics Core. The core will also maintain a centralized database of sequences and genotypes.
- ▶ Mass-spectrometry-based SNP genotyping or mutation detection, and DNA methylation studies, using the Sequenom MassARRAY and EpiTYPER platforms.
- ▶ Nanostring technology, which uses color-coded molecular barcodes that can hybridize directly to many different types of target molecules, and allows for a multiplexing level of detection of 800 targets simultaneously.



Kety Huberman, Senior Research Assistant



## JAMES HSIEH, MD, PhD

Faculty

### LAB MEMBERS

Yiyu Dong  
*Research Fellow*

Han Liu  
*Senior Research Scientist*

Edward Lu  
*Research Technician*

Shugaku Takeda  
*Research Fellow*

### SPOTLIGHT ON THE ACTIVITY OF MLL

#### Shugaku Takeda, PhD, Research Fellow

Dr. Shugaku Takeda is a Research Fellow at MSKCC, with specialties in developmental biology and oncology. He completed his doctoral thesis on MLL, an epigenetic transcription regulator, in Dr. James Hsieh's laboratory in 2010.

Dr. Takeda discovered a novel activity of MLL in the HGF-MET signaling pathway that is engaged in diverse biological processes, including cancer invasion and metastasis. Genetic and biochemical analyses demonstrated that HGF-MET coordinates the formation of MLL-ETS2 complex to allow upregulation of critical cell motility factors, such as MMP1. Dr. Takeda's studies not only identified previously unrecognized key epigenetic regulation in the HGF-MET signaling pathway, but also presented novel therapeutic strategies against cancer metastasis.

### RESEARCH FOCUS

Dr. Hsieh's lab focuses on decoding the molecular blueprint of cancers and developing novel cancer therapeutics.

The Hsieh lab discovered that the cellular oncogene MLL is regulated by site-specific proteolysis, which led to the purification of the responsible protease, which they named "Taspase1."

The discovery of Taspase1 initiated a novel class of endopeptidases. Taspase1 is an evolutionarily conserved protease that cleaves nuclear factors MLL and TFIIA to orchestrate fundamental biological events. It dictates cell fate, cell cycle, and stem and cancer cell biology, and functions as a non-oncogene addiction protease.

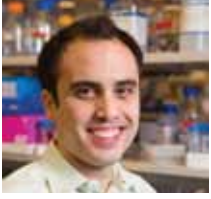
Accordingly, two ongoing research directions of the Hsieh laboratory are 1) to study the function of MLL and molecularly reconstruct human MLL leukemias, and 2) to study the function of Taspase1 in cancer pathogenesis and develop Taspase1 inhibitors for cancer therapeutics.

As Dr. Hsieh specializes in treating kidney cancers, the Hsieh lab will expand its research scope to establish a translational kidney cancer research component. The translational program will utilize patient materials to directly decode the molecular basis underlying treatment response and cancer metastasis, and thus offer personalized treatment regimens.

Furthermore, through building the molecular blueprint of kidney cancer pathogenesis, the lab wishes to develop novel mechanism-based therapeutics to better treat and eventually cure kidney cancer patients.



Yiyu Dong, Research Fellow



## JASON HUSE, MD, PhD

Affiliate Faculty

### LAB MEMBERS

Daniel Gorovets  
*Graduate Research Assistant*

Girish Harinath  
*Research Technician*

Edward Kastenhuber  
*Research Technician*

Joachim Silber  
*Research Fellow*

### SPOTLIGHT ON THE IMPACT OF MICRO-RNAS ON BRAIN TUMORS

#### Joachim Silber, PhD, Research Fellow

Dr. Joachim Silber is a Research Fellow in Dr. Jason Huse's laboratory at MSKCC studying brain cancer. He is particularly interested in the impact of microRNA-based gene regulation in the evolution of primary brain tumors.

MicroRNAs are a group of small RNA molecules that regulate genes by directly repressing their expression, and several microRNAs have been implicated in cancer. To explore the role of microRNAs in brain tumors, Dr. Silber is using a variety of in vitro techniques, as well as in vivo mouse models. Through his research, he hopes to identify pathogenic microRNA/mRNA interactions and the molecular networks in which they act, both of which may serve as targets for therapeutic intervention.

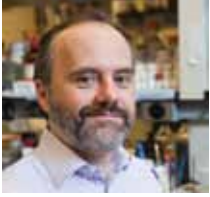
Dr. Silber recently received funding for his research, including salary support from the Lundbeck Foundation.

### RESEARCH FOCUS

Dr. Jason Huse is a neuropathologist who studies the pathophysiology of primary brain tumors, particularly diffuse gliomas. His research interests include miRNA biology and its involvement in brain tumorigenesis. He is also undertaking translational efforts linking molecular pathology with the implementation of clinical trials.



Edward Kastenhuber, Research Technician



## MARC LADANYI, MD

Faculty

### LAB MEMBERS

Nabahet Ameur  
*Research Fellow*

Laetitia Borsu  
*Genomics Project Manager*

Matthew Bott  
*Research Fellow*

Marie Brevet  
*Research Scholar*

Rafael Cabal  
*Senior Research Scientist*

Lishi Chen  
*Senior Research Assistant*

Yixuan Gong  
*Research Associate*

Tatsuo Ito  
*Research Scholar*

Rachel Kobos  
*Instructor*

Heather Magnan  
*Instructor*

Angela Marchetti  
*Research Technician*

Neal Shukla  
*Instructor*

Yoshiyuki Suehara  
*Visiting Investigator*

Lu Wang  
*Research Associate*

### SPOTLIGHT ON MUTATIONS IN THE BAP1 GENE IN MESOTHELIOMA

#### Matthew Bott, MD, Research Fellow

Dr. Matthew Bott is a resident in general surgery with an interest in tumors of the lung, esophagus, and chest cavity. He has now spent three years working in the Ladanyi lab, which focuses on using comprehensive genomic approaches to define the key genetic changes present in lung cancers, mesotheliomas, and sarcomas.

Dr. Bott's research recently discovered novel mutations in a gene called BAP1 in mesothelioma, a deadly tumor associated with exposure to asbestos. The lab has found that alterations in this gene are present in almost half of mesotheliomas.

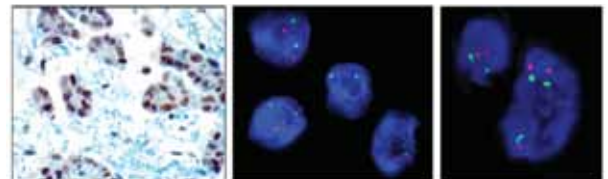
Over the past year, this work has been presented orally at major national and international meetings, such as the American Society of Clinical Oncology (ASCO) and the International Mesothelioma Interest Group. It was also published in *Nature Genetics*. The Ladanyi lab is currently working to understand how this discovery can be used to better treat patients with this devastating disease.

#### RESEARCH FOCUS

Dr. Ladanyi's research program focuses on the genomics and molecular pathogenesis of sarcomas and thoracic malignancies. A major focus is on the biology of human translocation-associated sarcomas.

Some of the recurrent themes of the research program include translocation breakpoint cloning and functional aspects of the chimeric transcription factors, using genome-wide location analysis (ChIP-Chip, ChIP-Seq) to define their target gene repertoires and relationships to histone modifications. Among sarcomas lacking recurrent translocations, embryonal rhabdomyosarcomas and osteosarcomas are the focus of new genomics efforts including whole exome and whole transcriptome sequencing, as well as focused mutational profiling based on the Sequenom mass spectrometry genotyping platform.

A second general area of work is in the genomics of thoracic malignancies, specifically mesothelioma and lung adenocarcinoma. Large integrated datasets of gene expression and copy number have been assembled and are being analyzed for relationships to known kinase mutations, for correlations with sensitivity to targeted therapies, and to uncover novel mutated cancer genes. Specific areas include defining and functionally validating the genes driving 8p12 losses and 1q21 gains in lung adenocarcinomas and 3p21 losses in mesothelioma, as well as defining correlates of kinase inhibitor sensitivity in mesotheliomas.



Left: Immunohistochemistry for BAP1 shows nuclear staining in a mesothelioma without BAP1 mutation. Center: Fluorescent in situ hybridization (FISH) analysis for BAP1 (red signals = BAP1 probe; green signals = chromosome 3 centromere) confirming loss of one copy of BAP1 in a mesothelioma sample. Right: FISH analysis for BAP1 showing two copies of BAP1 (normal pattern) in a mesothelioma without BAP1 alterations.





## ROSS LEVINE, MD

Faculty

### LAB MEMBERS

Omar Abdel-Wahab  
*Instructor*

Neha Bhagwat  
*Graduate Research Assistant – GSK*

Outi Kilpivaara  
*Research Fellow*

Priya Koppikar  
*Research Associate*

Nicole Kucine  
*Clinical Research Fellow*

Sachie Marubayashi  
*Research Technician, Sr.*

Suveg Pandey  
*Research Technician*

Jay Patel  
*Research Technician*

Raajit Rampal  
*Clinical Research Fellow*

Lindsay Saunders  
*Graduate Research Assistant – GSK*

Alison Schram  
*Graduate Research Assistant –  
U Penn (HHMI Research Fellow)*

Alan Shih  
*Clinical Research Fellow*

### SPOTLIGHT ON LEUKEMIA

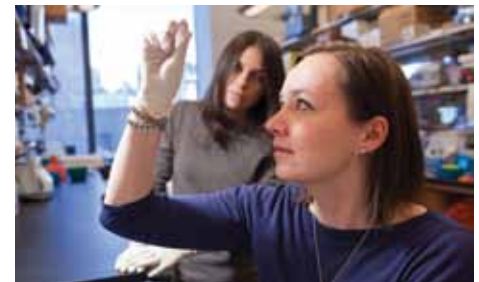
#### Omar Abdel-Wahab, MD, Instructor

Dr. Omar Abdel-Wahab is a medical oncologist specializing in the treatment of patients with leukemia. He joined Dr. Ross Levine’s lab with the hope of understanding more about the molecular underpinnings of leukemia. He was fortunate to join the lab at a time when genomic technologies are being heavily used to uncover genetic abnormalities in the malignant cells from patients with decreasing costs and increasing resolution.

Dr. Abdel-Wahab has been involved in the discovery and characterization of a series of new mutations in patients with acute and chronic leukemias, several of which appear to be promising targets for novel treatments.

### RESEARCH FOCUS

The focus of Dr. Levine’s work is to improve our understanding of the genetic basis of myeloid malignancies, with a specific focus on the role of oncogenic disease alleles in the pathogenesis of the BCR-ABL-negative myeloproliferative neoplasms (MPN), polycythemia vera (PV), essential thrombocytosis (ET), and primary myelofibrosis (PMF).



Outi Kilpivaara, Research Fellow, and Alison Schram, Graduate Research Assistant

As a postdoctoral fellow in Gary Gilliland’s lab, Dr. Levine used high-throughput sequence analysis of the tyrosine kinome to identify JAK2V617F mutations in most patients with PV, and in a significant proportion of patients with ET and PMF, as well as MPLW515L/K mutations in some patients with JAK2V617F-negative ET and PMF and JAK2 exon 12 mutations in patients with JAK2V617F-negative PV.

More recently, Dr. Levine’s lab has identified inherited disease alleles relevant to MPN pathogenesis and characterized the effects of targeted therapies on signaling and outcome in MPN mouse models.

Dr. Levine’s current efforts are focused on the following areas:

- ▶ Identification of somatic mutations that activate signal transduction in JAK2V617F-negative MPD, using candidate gene, genome-wide, and functional approaches.
- ▶ Investigation of the role of different signaling pathways in hematopoietic transformation by activating mutations in JAK2 and MPL.
- ▶ Investigation of the role of inherited disease alleles in MPN pathogenesis.
- ▶ Characterization of inhibitors of JAK2 kinase activity with a potential role in the treatment of PV, ET, and PMF using in vitro and in vivo assays, and elucidation of the mechanisms of resistance to JAK2 inhibitors using in vitro systems to develop additional novel therapies for MPN patients.
- ▶ Development of novel genetic screens to identify additional oncogenic alleles in hematopoietic malignancies with pathogenetic and therapeutic significance.





## INGO MELLINGHOFF, MD

Faculty

### LAB MEMBERS

Carl Campos  
*Research Assistant*

Milan Chheda  
*Instructor*

Christian Grommes  
*Clinical Research Fellow*

Sara Kubek  
*Graduate Research Assistant – Cornell*

Barbara Oldrini  
*Research Fellow*

Daniel Rohle  
*Graduate Research Assistant – Cornell*

Igor Vivanco  
*Research Associate*

Nicolas Yannuzzi  
*Volunteer*

### SPOTLIGHT ON EGFR-MUTANT BRAIN CANCER

#### Igor Vivanco, PhD, Research Associate

Dr. Igor Vivanco is a research associate in the Mellinghoff lab, where he focuses on the study of glioblastoma, the most aggressive form of primary brain cancer. Dr. Vivanco works on optimizing the use of a class of cancer drugs (or inhibitors) that specifically switch off the function of a protein, called epidermal growth factor receptor (or EGFR), commonly mutated in brain cancer.

The Mellinghoff lab has recently discovered that the loss of a gene called PTEN in cancer cells with EGFR mutations can severely restrain the efficacy of EGFR inhibitors by increasing the activity of EGFR. This increase in activity, in turn, requires that a higher amount of drug be administered to turn off EGFR. This discovery implies that brain cancer patients can still benefit from EGFR inhibitor treatment, but new dose schedules will need to be implemented for tumors that have lost PTEN, a very common occurrence in EGFR-mutant brain cancer.

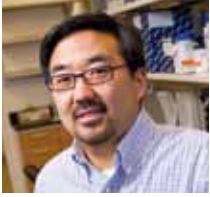
These results were published in the Proceedings of the National Academy of Sciences in March of 2010, and have led to the design of a clinical trial for glioblastoma patients to be treated with high amounts of the EGFR inhibitor erlotinib.

### RESEARCH FOCUS

Dr. Mellinghoff's research focuses on glioblastoma (GBM), which is the most common malignant brain tumor in adults, with a median survival of 15 months despite therapy with radiation and chemotherapy.

Dr. Mellinghoff's present efforts are in the following areas:

- ▶ Further exploration of the EGFR signaling axis in glioma. This project aims to further elucidate two of Dr. Mellinghoff's recent clinical observations in GBM, namely the presence of extracellular EGFR missense mutations in about 10% of GBMs and the strong association between PTEN loss and clinical resistance to EGFR kinase inhibitor therapy. The goal of the Mellinghoff lab's current studies is to define the contribution of the new EGFR missense mutations in glioma formation/maintenance and unravel and overcome the molecular basis of PTEN-associated EGFR kinase inhibitor resistance.
- ▶ Functional validation of potential new therapeutic targets in glioblastoma identified through a recent survey of the cancer genome in glioblastoma patient samples. In collaboration with Dr. Cameron Brennan, the Mellinghoff lab derived a number of short-term cultures from MSKCC GBM patients. The lab members have profiled them for signature mutations in GBM and are now manipulating individual genes using inducible cDNA or shRNA alleles.
- ▶ Conducting early-phase clinical trials with signal transduction inhibitors for glioma, with particular emphasis on genotype-based enrollment and monitoring of target inhibition in tumor tissue.



## CHRISTOPHER PARK, MD, PhD

Faculty

### LAB MEMBERS

Rashmi Bhardwaj  
*Research Fellow*

Stephan Chung  
*Clinical Research Fellow*

Jia Fei  
*Visiting Investigator*

Wenhao Hu  
*Research Fellow*

Rina Meyer  
*Clinical Research Fellow*

Allison Rainey  
*Research Technician, Sr.*

### SPOTLIGHT ON MYELOYDYSPLASTIC SYNDROMES

#### Rashmi Bhardwaj, PhD, Research Scholar

Dr. Rashmi Bhardwaj is a Research Scholar at MSKCC, with research interest in blood disorders and stem cells. She recently received her PhD in the Department of Medical Oncology, All India Institute of Medical Sciences, for work on the regulation of human fetal liver blood stem cell growth. She joined Dr. Park's lab in February 2010 and now works on the molecular biology of myelodysplastic syndromes (MDS), a group of bone marrow failure syndromes primarily affecting older adults and those treated for cancers.

MDS results in disorderly and ineffective blood production, manifested by defects in blood-forming cells. Dr. Bhardwaj's work involves purifying blood stem cell populations from MDS patients and mouse models of MDS and studying their unique biological properties.

Currently, Dr. Bhardwaj is investigating the roles of altered cellular metabolism and protein synthesis in the development and progression of these disorders.

### RESEARCH FOCUS

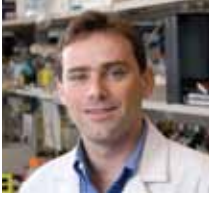
Dr. Park's research focuses on the molecular mechanisms that regulate stem cells in normal and neoplastic hematopoiesis. As a Post Doctoral Fellow in Irving Weissman's lab, Dr. Park analyzed microRNA expression patterns in purified human hematopoietic stem cells (HSC) and committed progenitors, as well as leukemia-initiating cells, in human acute myeloid leukemia (AML).

These studies revealed widespread miRNA dysregulation in AML compared with normal HSC/committed progenitors and resulted in the demonstration that enforced expression of miR-29a in mouse hematopoietic stem/progenitor cells was sufficient to induce a myeloproliferative disorder that progressed to frank AML, strongly suggesting that miR-29a is an oncogenic microRNA in human AML.

Dr. Park also investigates the cellular and molecular basis of bone marrow failure syndromes, specifically myelodysplastic syndromes. Having performed transcriptome analysis of purified HSC and committed progenitors from a large number of MDS patients, Dr. Park has identified widespread dysregulated mRNA expression differences in HSC, including numerous cell-surface proteins and components of the ribosome machinery.

Current areas of investigation include the following:

- ▶ Cellular and molecular basis of miR-29a's leukemogenic activity using mouse models and primary AML xenografts
- ▶ Characterization of additional candidate miRNA oncogenes and tumor suppressors in normal hematopoiesis and AML
- ▶ Mechanisms regulating hematopoietic cells competition (HSC) and cell death in myelodysplastic syndrome (MDS), using both mouse models and primary patient samples
- ▶ Evaluation of cell surface molecules identified in MDS HSC for their suitability as diagnostic/prognostic markers, as therapeutic targets, and as a means for prospectively separating neoplastic from normal HSC in MDS samples



## DAVID SOLIT, MD

Faculty

### LAB MEMBERS

Julian Agin-Liebse  
*Research Technician*

Federica Catalanotti  
*Research Fellow*

Aphrothiti Hanrahan  
*Research Scholar*

Gopakumar Iyer  
*Clinical Research Fellow*

Manickam Janakiraman  
*Research Fellow*

Li Kong  
*Research Fellow*

Moriah Nissan  
*Graduate Research Assistant – GSK*

Yogindra Persaud  
*Research Technician, Sr.*

Efsevia Vakiani  
*Assistant Attending*

Feng Xing  
*Research Scholar*

### SPOTLIGHT ON OVARIAN CANCER

#### Aphrothiti Hanrahan, PhD, Research Scholar

Dr. Aphrothiti Hanrahan is a Postdoctoral Research Scholar at MSKCC, with a research focus on ovarian cancer, a complex disease lacking a hallmark, causal genetic event.

Frequently, genes in the PI3k/AKT signaling cascade, which contribute to cell growth and survival, are over-activated in ovarian cancer, suggesting that ovarian tumors may respond to drugs blocking this pathway.

In collaboration with Dr. Douglas Levine, a surgeon on MSKCC's Gynecology Service, MSKCC's Computational Biology Center and several core facilities, and The Cancer Genome Atlas project on ovarian cancer, the Solit lab analyzed a large set of ovarian cancer cell lines and ovarian tumors with the goal of defining genetic mutations that predict sensitivity to inhibitors of AKT signaling. AKT pathway alterations were common, but insufficient to confer sensitivity to AKT inhibitors. Tumor cells expressing genetic changes in the genes RAS or RB1, which are found in many cancers, were resistant to AKT inhibition.

In summary, a subset of ovarian tumors exhibit AKT dependence, but the genetic complexity of this disease suggests that effective treatment of ovarian cancer patients with targeted inhibitors will require a personalized approach based on detailed genetic characterization of individual tumors.

### RESEARCH FOCUS

Dr. Solit has focused his research on inhibiting critical signaling pathways that promote tumorigenesis. He was a leader in investigating Hsp90 inhibitors in tumors driven by oncogenic AKT or BRAF and served as the lead investigator on a phase I trial of 17-AAG in patients with advanced solid tumor malignancies and a phase II trial of 17-AAG in patients with metastatic melanoma.

Dr. Solit was the first to show that tumors with BRAF mutation are selectively sensitive to MEK inhibition as compared with tumors in which the pathway is activated by either RAS mutation or mutation/amplification of upstream receptor tyrosine kinases. This data has served as the basis for an ongoing phase II trial with AZD6244 in melanoma patients with mutated BRAF.

Dr. Solit's recent lab work has focused on the identification of mutational events that cooperate with mutant BRAF in melanomagenesis and abrogate BRAF addiction. His research group has also been active in the development of novel methods to genetically profile formalin-fixed paraffin-embedded tissues for somatic mutations and copy number alterations.



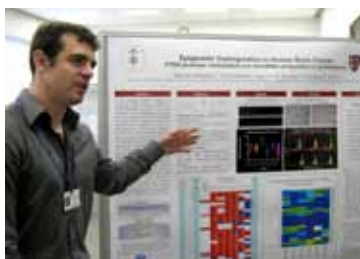
Federica Catalanotti, Research Fellow

## Prepping the next generation of physician-scientists and collaborative researchers

### SUMMER STUDENT PROGRAM

In 2010, HOPP established a formal Summer Student Program geared toward providing students at all educational levels a chance to participate in a structured educational lab experience. The program provides students with an opportunity to work on a translational research project, learn new laboratory techniques, and participate in weekly events that enrich their interactions with HOPP faculty, lab members, and other MSKCC Summer Students.

The 2010 program cultivated the minds of 24 students (7 high school, 13 college, 4 MD/PhD).



Marcus Alexander, MD/PhD student in the Huse lab



Summer students attending orientation

"I just learned so much. The learning was incredible and the technology was really advanced. I thoroughly enjoyed all the interactions with the people in my lab, and learning about the experiments."

– David Ajasin (Brennan lab)

"I enjoyed seeing the connection between the theories that I'm learning at school in chemistry and biology, and how it is used in the labs."

– Gbambele Kone (Park lab)

"I got to shadow Dr. Daniel Danila in the clinic, which was awesome. I realized the MD/PhD path is not just research; it has a clinical part as well."

– Angela Su (Sawyers lab)

### HIGH SCHOOL OUTREACH

In 2006, Memorial Sloan-Kettering established an annual symposium designed to expose members of the public, especially high school students, to important new research that is contributing to the understanding and treatment of cancer.

Every year, "*Major Trends in Modern Cancer Research*" features a group of the Center's leading scientists presenting their work to high school students and secondary school science teachers, offering a chance for them to interact and ask questions about Memorial Sloan-Kettering's research and the latest advances in biomedical research.

This year, HOPP faculty member Dr. Timothy Chan was selected as a speaker, and, to support MSKCC's goal to shape and inspire future scientists, provided a group of students from Essex Street Academy the opportunity to visit his lab and obtain some background information on his talk, as well as cancer research.



Dr. Timothy Chan speaking with students from Essex Street Academy



"The visit was very rewarding on my end because it was a great opportunity to expose high school students to the excitement of science early in their education. Many of the students expressed strong interest in learning about careers in the medical sciences. We spent a lot of time discussing different ways to pursue a career in science. We then toured the labs, examined how some of the equipment we use works, and looked at cancer cells through the microscope. It was very rewarding to hear some of the students that day say they wanted to do this in the future."

– Dr. Timothy Chan



## HOPP RESEARCH SEMINAR SERIES

The HOPP Research Seminar Series (RSS) was created as a venue to provide HOPP and other investigators in the institution with an opportunity to learn about cutting-edge translational research being conducted by other senior researchers around the world.

Speakers are all from outside MSKCC and are carefully selected by the RSS Chair, Dr. Ross Levine, and our Program Chair, Dr. Charles Sawyers. The audience typically consists of investigators and lab members throughout the institution.

The RSS is in its third year and draws in more than 85 attendees.



Yardena Samuels  
Speaker on April 28, 2011



Jean Pierre Issa  
Speaker on Feb 24, 2011



HOPP Research Seminar attendees

## 2010-2011 RESEARCH SEMINAR SERIES SCHEDULE

| DATE               | SPEAKER   | INSTITUTION                                   | HOST                            |
|--------------------|---|---|---------------------------------|
| September 30, 2010 | Sridhar Ramaswamy, MD<br>– Assistant Professor of Medicine, Harvard Medical School<br>– Tucker Gosnell Investigator, Massachusetts General Hospital Cancer Center   | Massachusetts General Hospital                | Charles Sawyers                 |
| October 28, 2010   | Norman E. Sharpless, MD<br>– Associate Professor of Medicine & Genetics<br>– The Lineberger Comprehensive Cancer Center   | University of North Carolina                  | Ingo Mellinghoff                |
| November 9, 2010   | Dean W. Felsher, MD, PhD<br>– Associate Professor, Medicine – Oncology<br>– Associate Professor, Pathology<br>– Member, Bio-X<br>– Member, Cancer Center  | Stanford University                           | Charles Sawyers                 |
| December 16, 2010  | Charles B. Smith Visiting Research Professor Co-Hosted w/ Dept. Medicine<br>Helen M. Piwnicka-Worms, PhD<br>– Professor, Cell Biology and Physiology & Internal Medicine<br>– Investigator, Howard Hughes Medical Institute                             | Washington University in St. Louis            | George Bosl and Charles Sawyers |
| January 27, 2011   | Jeff Engelman, MD, PhD<br>– Assistant Professor, Department of Medicine, Harvard Medical School<br>– Assistant Physician, Medical Oncology, Massachusetts General Hospital  | Massachusetts General Hospital                | Charles Sawyers                 |
| February 24, 2011  | Jean Pierre Issa, MD<br>– Professor, American Cancer Society of Clinical Research<br>– Co-Director, Center for Cancer Epigenetics, Institute of Basic Science Research<br>– Professor, Department of Leukemia; Chief, Section of Translational Research | University of Texas MD Anderson Cancer Center | Timothy Chan                    |
| March 31, 2011     | Terry Rabbits, PhD, FRS, FMedSci<br>– Director, Leeds Institute of Molecular Medicine   | Leeds Institute of Molecular Medicine         | James Hsieh                     |
| April 28, 2011     | Yardena Samuels, PhD<br>– Investigator, Cancer Genetics Branch<br>– Head, Molecular Cancer Genetics Section   | National Human Genome Research Institute      | David Solit                     |
| May 26, 2011       | Adrienne Cox, PhD<br>– Associate Professor, Department of Radiation Oncology  | University of North Carolina                  | Charles Sawyers                 |
| June 30, 2011      | Danilo Perrotti, MD, PhD<br>– Associate Professor, Molecular Virology, Immunology & Medical Genetics  | Ohio State University                         | Ross Levine                     |



SPOTLIGHT ON DR. ROSS LEVINE

TRAINING FOR PROGRESS

“It’s an opportunity for trainees to be exposed to cutting-edge research that helps their development.”

Dr. Ross Levine is a prominent member of HOPP. His work in the field of hematopoietic malignancies has made him an important contributor to HOPP’s mission in training future physician-scientists. He’s been the RSS Chair since 2009 and is proud to see what it has become.

Our seminar series has been very successful within HOPP and MSKCC, and has provided another opportunity to showcase translational research. We’ve provided a forum for national leaders in translational oncology research to come to Memorial to present their work to both clinical and research faculty.

The HOPP RSS provides the department and the greater MSKCC community a chance to really think about trainees. It’s an opportunity for trainees to be exposed to cutting-edge research that helps their development. Our seminars can help them understand different approaches and provide insights into their decision making.



Alison Schram, Graduate Research Assistant



Sachie Marubayashi, Research Technician



Suveg Pandey, Research Technician



Raajit Rampal, Clinical Research Fellow



Lindsay Saunders, Graduate Research Assistant

## HUMAN ONCOLOGY & PATHOGENESIS PROGRAM (HOPP) AND CANCER BIOLOGY & GENETICS (CBG) SCIENCE CLUB

This science club meeting brings together members from HOPP and CBG with the goals of promoting program interactions and giving trainees more experience with making presentations. The meetings allow both programs to hear about the ongoing research being conducted in their labs.

Science Club is held every Thursday starting in October and ending in June. The meetings are approximately one hour and consist of two presentations—one from HOPP and one from CBG. Presenters are typically trainees or junior faculty from each of these programs, though occasionally the schedule does include guest speakers from Memorial Hospital and other SKI programs with overlapping research interests.

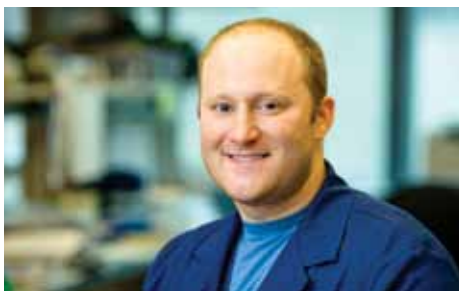
“Science club is a terrific forum for faculty and trainees in HOPP and CBG to exchange ideas on a weekly basis. I am particularly delighted by the many collaborations that have emerged from these meetings.”

– Dr. Sawyers



“Science club is a great opportunity to hear what our colleagues are working on. It provides for interesting discussions, covers a wide variety of topics, and I always learn something.”

– Nicole Kucine, Clinical Research Fellow (Levine Lab)



“Science club provides the chance to see the different areas that your peers are researching, which can open doors to new collaborations, finding needed reagents/techniques, and potentially taking your own research in a completely different direction.”

– Daniel Rohle, Graduate Research Fellow (Mellinghoff Lab)

### 2010–2011 SCHEDULE

| DATE        | DEPT        | LAB HEAD                  | PRESENTER  | TITLE  |
|-------------|-------------|---------------------------|--|--|
| October 7   | CBG<br>HOPP | Massagué<br>Sawyers       | Thordur Oskarsson<br>Yu Chen                         | Research Associate<br>Special Fellow             |
| October 14  | HOPP<br>CBG | Solit<br>Benezra          | Gopa Iyer<br>Juan M. Schwartzman                     | Clinical Research Fellow<br>Graduate Student     |
| October 21  | CBG<br>HOPP | Holland<br>Levine         | Rebecca Bish<br>Omar Abdel-Wahab                     | Research Scholar<br>Clinical Research Fellow     |
| November 4  | HOPP<br>CBG | Guest Speaker<br>Joyce    | Douglas Levine<br>Hao-Wei Wang                       | Associate Attending<br>Graduate Student          |
| November 11 | CBG<br>HOPP | Kenney<br>Huse            | Bipin Bhatia<br>Joachim Silber                       | Research Associate<br>Research Fellow            |
| November 18 | HOPP<br>CBG | Chan<br>Klein             | Luc Morris<br>Xing (Dandan) Xu                       | Clinical Research Fellow<br>Graduate Student     |
| December 9  | CBG<br>HOPP | Massagué<br>Guest Speaker | Sakari Vanharant<br>Chris Sander Lab<br>Ethan Cerami | Research Scholar<br>Computational Biology Center |
| December 16 | HOPP<br>CBG | Ladanyi<br>Wendel         | Nahabet Ameer<br>Konstantinos Mavrakis               | Research Fellow<br>Research Fellow               |
| January 6   | CBG<br>HOPP | Offit<br>Levine           | Vijai Joseph<br>Neha Bhagwat                         | Research Fellow<br>Graduate Research Assistant   |



Staff contribute to research outside of the workplace

**CYCLE FOR SURVIVAL**

**Camille Teta, Research Secretary**

Camille Teta participated in the Cycle for Survival event on January 31, 2010.

**What is Cycle for Survival?**

Cycle for Survival is an MSKCC fundraising event through which teams raise money by spinning. Since spinning is a stationary form of cycling, the event was held indoors at Equinox Gym in Midtown in New York City. Our instructors position themselves in the center of the floor, with half the riders on one side, and half on the other. Team members take turns riding the bikes.

There was a great meeting area with food and giveaways, which gave people a chance to socialize and learn more about each other. The event started at 7 AM and lasted until about noon. Each team was assigned a certain amount of bikes, so team members cycled based on rotations and everyone got to ride at least twice. My team was made up of about 12 people.

**Would you participate in something like this again?**

Yes, absolutely. I was able to participate in an awesome activity with great team



Camille Teta, Research Secretary

members. We came together to focus on and raise awareness about cancer research. I got to meet new people who care about the same things that I do. Also, I loved the energy! The instructors were awesome and kept us pumped up.

**How does HOPP's mission motivate your passion and desire to participate in these activities?**

We come from an atmosphere that stands for unity against cancer. Cycle for Survival is the type of event that motivates you to think about how we translate the research into the clinic, and if you can be a part of an event that can fundraise towards that goal, it's definitely rewarding.

When you consider the mission of the program, you realize how important it is to

have the funding in order to continue this research and bring it to the patients. There is a lot of potential in HOPP, and here everyone works together toward the long-term goal of the department. Every effort is a reward in itself, and we contribute toward funding the helpful results brought from the laboratories to the patients.

Learn more about Cycle for Survival at [www.cycleforsurvival.org](http://www.cycleforsurvival.org)



Cycle for Survival participants



**VOLUNTEER: DEPARTMENT OF PEDIATRICS**

**Lorraine Pistorino, Program/Fund Coordinator**

**Tell us about your volunteer experience in Pediatrics.**

I volunteer in Pediatrics Department on Wednesdays during the swing shift, late afternoon to early evening. What I like about this shift is that I am able to see both outpatients and inpatients. I spend the first half of my time in the outpatient recreation room, playing games and doing crafts with the patients and their siblings. Toward the end of the shift after the rec room closes, I visit the inpatient rooms. A lot of inpatient

kids are in isolation; they're either pre- or post- bone marrow transplant or just highly susceptible to germs so they cannot leave their rooms. As volunteers we are able to spend time with them and give them the individualized attention they need.

**Why did you do this and would you participate again?**

I have wanted to volunteer since I started working at MSK, but more recently I felt the need to become involved on the clinical

## OVAC HILL DAY

**Aime Franco, Postdoctoral Fellow**

**Please tell us about your recent involvement in OVAC (One Voice Against Cancer) through the AACR.**

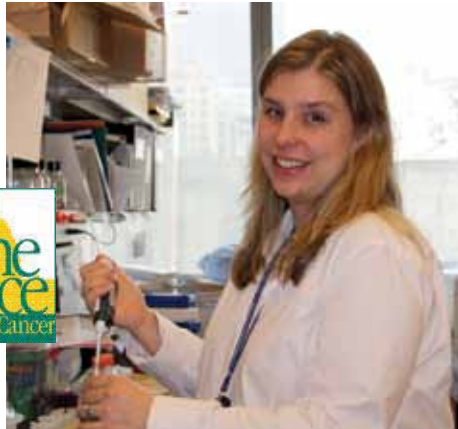
I participated in the OVAC Hill Day, which is a two-day event held in Washington, D.C. We met with several cancer advocates, survivors, and researchers to learn about what we were going to do on the Hill with our Congressmen and women, and Representatives. Representatives came in to talk to our group and give us an overview of government, along with a brief lesson about how a bill becomes a law.

The second day we went to Capitol Hill. I was part of the New York Contingent and visited the offices of Senator Chuck Schumer, Senator Kristen Gillibrand, and also Representative Carolyn Maloney. We went to their offices and gave them packets explaining what we were lobbying for:

- keeping NIH funding at its current level
- increasing FDA awareness on approving cancer-related drugs and stopping the roadblocks in the drug-approval process
- keeping funding in CDC programs for prevention and awareness
- fully funding the Caroline Pryce Walker Conquer Childhood Cancer Act

side and have one-on-one interaction with the patients. The shared goal of all our jobs is to better the lives of the patients and that's what motivates me to work at a place like MSKCC. I have a lot of experience with children and really enjoy spending time with them, so I wanted to volunteer in Pediatrics.

I value and appreciate the opportunity to spend time with these kids — their maturity, resilience, and strength are inspiring. They're constantly making me smile and laugh. I told one six-year-old girl (who had been in the hospital for months) that her doll's outfit was something I'd wear and she responded with, "I don't



Aime Franco, Research Fellow

- keeping funding for nurse programs to prevent shortages in areas that specifically relate to cancer treatment

**Would you participate in something like this again?**

Yes! I never thought that my voice could make a difference in government, or that writing letters ever impacted anything. From this experience, I realized firsthand that I can make a difference.

I've got to be actively involved. Wanting to go into academia, if I'm unable to obtain funding, I won't have a career; this was the perspective I brought to our representatives. If funding ends now, you stop the pipeline. It's people like me who are training and looking for jobs who are greatly impacted by the loss of funding. Not only does lack

think that comes in your size!" It's been an amazing and life-changing experience for me. I have met a few people who have been volunteering for more than 20 years and I hope to be in Pediatrics just as long as them.

**How does HOPP's mission motivate your passion and desire to participate in these activities?**

Sitting in the Zuckerman research building can sometimes feel isolating from the clinical environment. However, in HOPP we are exposed to the clinical side because our scientists are also physicians who see

of funding slow things down, it stops the initiative and innovation, in addition to preventing an entire new generation of researchers from pursuing their goals. I want to keep doing this and continue to be on the forefront of translational medicine. As a PhD, I apply what I'm doing in D.C. to my experience in HOPP.

**How does HOPP's mission motivate your passion and desire to participate in these activities?**

I see the advances we are making and how we can apply them to patient care. I see exactly how what we are doing in the lab applies to the clinic.

For example, in Dr. Fagin's lab, we have the thyroid working group. Clinicians come to the lab meetings and want to know what we are doing and how they can apply it to their patients. I work in the lab and can see where it's all going and how desperately we need the funding, training, and representation from all levels of scientists out there in D.C. I worry that funding won't continue unless we get the support we need from the government. Being able to really see how I can translate the basic science into the clinic shows how important lobbying is.

Learn more about Aime and OVAC by visiting [www.aacr.org](http://www.aacr.org) and read her story in the AACR Cancer Policy Monitor (July 2010 edition).

patients. I think that fosters the interest in learning more about the clinic.

Although each of us has an impact on the overall mission of MSKCC, I wanted to be on the front end as opposed to solely providing administrative support on the back end. So as an employee I am proud to be a volunteer but the opposite is also true; as a volunteer I am proud to be a member of HOPP. I have a unique perspective that I have learned to appreciate — I am able to see the needs of the patient but also see how passionate and motivated the researchers are in developing better treatments for the patients.



HOPP is a marriage of collaboration and cancer research

**SHAREPOINT**

The HOPP SharePoint site launched over the summer. The site's creation came at an ideal time, supporting communication for our rapidly growing program. The site provides the laboratories with a central place to share and house information that is easily accessible and important for keeping labs on different floors in contact with one another. The site supports collaboration by giving researchers a chance to interact with current members of the department and identify resources, and it is also an effective and efficient way to welcome the newest members of the program.



**WORK IN PROGRESS MEETINGS**

The purpose of Work in Progress meetings is to give HOPP faculty a chance to update one another on their ongoing work. During these weekly meetings, there is one speaker who gives an informal presentation about his or her lab work. All HOPP Principal Investigators are invited to attend and present, as well several outside SKI and clinical faculty with overlapping interests.

| 2010-2011 SCHEDULE |             |            |           |         |           |
|--------------------|-------------|------------|-----------|---------|-----------|
| September 29       | Sawyers     | December 8 | Solit     | March 2 | Nimer     |
|                    |             | 14         | Cheng     | 16      | D. Levine |
|                    |             |            |           | 30      | Bromberg  |
| October 6          | Holland     | January 5  | Park      | April 6 | Sander    |
| 13                 | Mellinghoff | 12         | Lash      | 13      | Antonescu |
| 20                 | Chan        | 19         | Lash      | 20      | Heguy     |
| 27                 | Ladanyi     |            |           | 27      | Bastian   |
| November 3         | Hsieh       | February 9 | Socci     | May 4   | Brennan   |
| 10                 | Fagin       | 16         | Djaballah | 11      | Sawyers   |
| 17                 | Levine      | 23         | Huse      | 18      | Viale     |
|                    |             |            |           | 25      | King      |



**EXTERNAL ADVISORY BOARD**

To maximize the resources and advantages found in a unique program like HOPP, Dr. Charles Sawyers seeks advice from a world-renowned panel of research experts—the HOPP External Advisory Board (EAB). The EAB provides Dr. Sawyers with invaluable input on the strategic planning for the program. The committee members assist him by identifying outstanding young recruits, providing information on the latest technology and research trends, and evaluating the research portfolios of our HOPP faculty members and core facility leadership.

**EXTERNAL ADVISORY BOARD MEMBERS**

[Lynda Chin](#)  
Professor of Dermatology  
Dana-Farber Cancer Institute

[Kathleen Cho](#)  
Peter A. Ward Professor of Pathology  
Professor, Depts of Pathology and Internal Medicine  
University of Michigan

[James Downing](#)  
Scientific Director & EVP  
St. Jude Children's Research Hospital

[Todd Golub](#)  
Professor of Pediatrics  
Dana-Farber Cancer Institute

[William G. Kaelin, Jr.](#)  
Professor of Medicine  
Dana-Farber Cancer Institute

[Steven Leach](#)  
Professor of Surgery and Oncology  
Johns Hopkins University

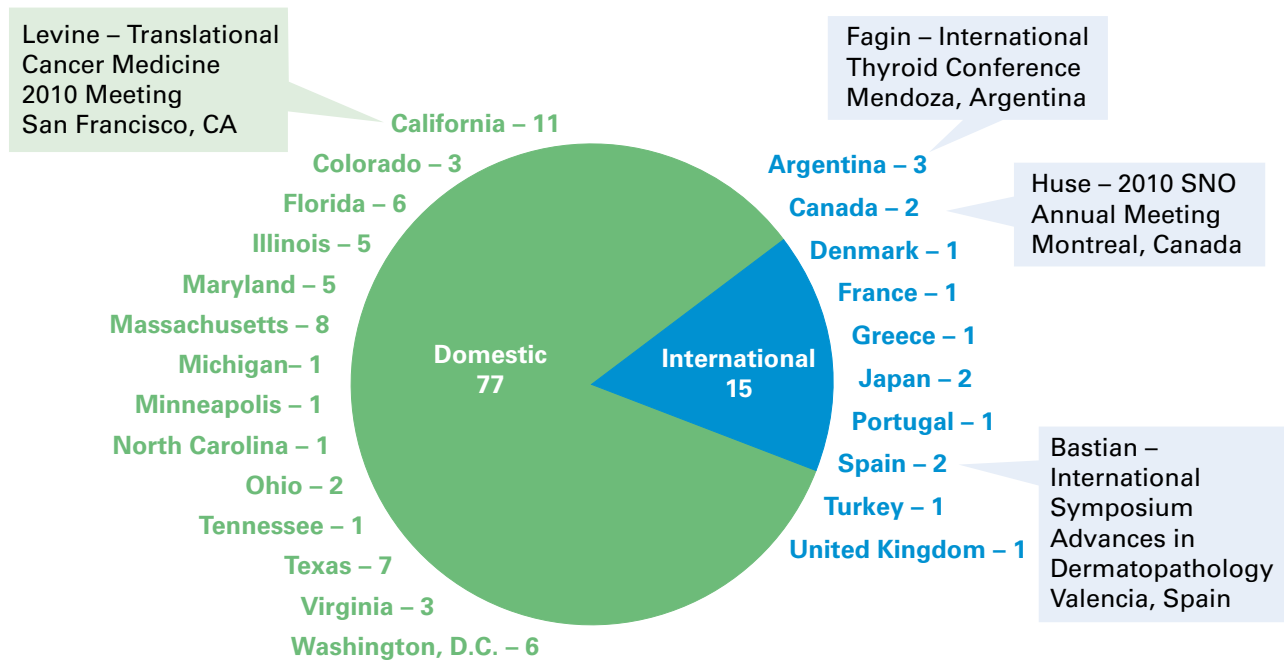
[Sanford Markowitz](#)  
Markowitz-Ingalls Professor of Cancer Genetics  
Case Comprehensive Cancer Center

[Kevin Shannon](#)  
(EAB Chairman)  
Professor of Pediatrics  
University of California, San Francisco

## FACULTY COLLABORATIVE EFFORTS

### SEMINARS

In 2010, our faculty were actively traveling the world and sharing their research findings with other institutions. They were solicited for a variety of different speaking engagements. Below is a chart representing our faculty's continual involvement in opening the door for future collaborations across the globe.



### PROFESSIONAL MEMBERSHIPS/ACTIVITIES

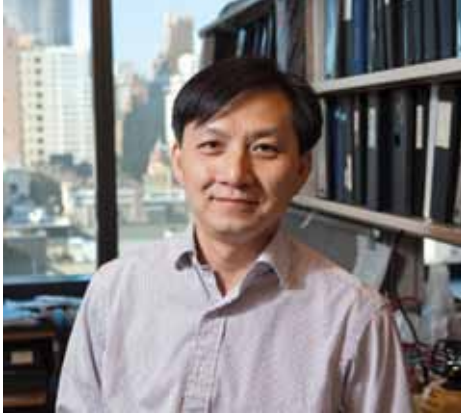
HOPP faculty continue to be at the forefront of sustaining collaboration among clinicians and other researchers. Their ability to fit into various team settings is directly linked to their participation in extramural activities. Listed below are professional memberships and other activities of HOPP faculty that cross over into other areas in clinical research and basic science.

Selected 2010 memberships:

|              |  |
|--------------|--|
| Timothy Chan | Disease Working Group, Colorectal Disease; The Cancer Genome Atlas project (TCGA); Scientific Advisory Board, Cancer Genetics Inc. |
| David Solit  | NCI SEP; Drug Discovery, Chemoprevention and Targeted Therapy, ZCA1 GRB-P01; Geoffrey Beene Cancer Research Center and Foundation  |
| James Fagin  | Thyroid Program Task Force Planning Committee; Endocrine Chief Search Committee (Cornell)  |

## CREATING COLLABORATIVE ENVIRONMENTS

“HOPP is the ideal program to bridge things together. We are the translational component.”



When Dr. Hsieh started seeing kidney cancer patients, there were no effective, nontoxic drugs. The clinical aspect was miserable since most kidney cancer patients failed to respond to available treatment at that time. With modern targeted therapy, many patients benefited but eventually relapsed. Dr. Hsieh knew more had to be done to understand this dreadful illness. He brought a new vision to HOPP—an integrated approach to the study and treatment of kidney cancer.

“There are many great physicians at MSKCC who primarily focus on the clinical aspects of kidney cancer. Robert Motzer’s clinical trials paradigm shifted the way we treat metastatic kidney cancer. The work of Drs. Reuter and Russo, a world-renowned GU pathologist and urological surgeon, respectively, defines current classification and surgical management of kidney cancer.

“However, there is a lack of a comprehensive translational platform to integrate everyone’s clinical efforts and interests. HOPP is the ideal program to bridge everyone together, and we provide the missing translational component. I want to bring everyone together to work as a team. We have established a monthly translational meeting where clinicians, pathologists, surgeons, radiologists, and scientists rotate to present their ideas and data.

“We need to formulate a scientific basis to better kidney cancer treatment because cancer is a heterogeneous disease that should not be treated homogeneously. Furthermore, not everyone responds to treatment. We need to come up with new treatment programs.”



Dr. James Hsieh discussing his vision for kidney cancer care at the first Work in Progress meeting.

## RESEARCH WITH OTHER INSTITUTIONS

In addition to carrying out independent projects, the faculty members in HOPP are well integrated into the scientific and clinical communities both inside and outside of MSKCC.

Here are a few examples of how HOPP is involved with the research community:

### STAND UP TO CANCER DREAM TEAM



Despite recent advances in therapies for breast cancers, nearly half a million women die of this disease annually worldwide. While ovarian and endometrial cancers are less common than breast cancers, nearly 65% of women with ovarian cancer die from this disease, and women diagnosed with advanced-stage endometrial cancers also have very high mortality rates.

Recent studies indicate that these three cancers have in common frequent mutations in a set of genes that regulate a cancer pathway, called the PI3K pathway.

The scientists who have been assembled for this Dream Team are the pioneers who discovered the PI3K pathway and who have validated its role in human cancers. HOPP investigators are teaming up with other clinical departments at Memorial Sloan-Kettering and four other institutions (Dana Farber/Harvard Cancer Center, M.D. Anderson Cancer Center, Vanderbilt Ingram Cancer Center, and Vall d'Hebron Oncology Research Institute) in this endeavor.

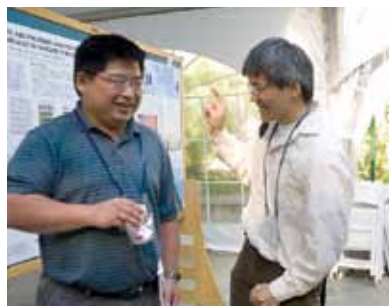
One hypothesis being tested by this team is that, since PI3K pathway mutations are frequent in breast, ovarian, and endometrial cancers, a common set of techniques may be successful at predicting patients who will benefit from PI3K pathway inhibitors in all three of these diseases. Thus, we are taking the unprecedented approach of collaborating not only across multiple institutions but also across multiple diseases. Our hope is that by encouraging the exchange of materials and ideas between scientists and clinicians working in these three diseases, we will accelerate the cure of all three.

For more information visit [www.standup2cancer.org](http://www.standup2cancer.org).

### STARR CANCER CONSORTIUM

The Starr Cancer Consortium (SCC) was established in 2006 through a generous gift from the Starr Foundation to advance research in new ways that will have an impact on the understanding, diagnosis, prevention, and treatment of cancer. The SCC is a collaborative frame work between five institutions—Memorial Sloan-Kettering Cancer Center, the Broad Institute of MIT and Harvard, Cold Spring Harbor Laboratory, The Rockefeller University, and Weill Cornell Medical College.

HOPP investigators have been very successful in receiving STARR grant awards since the consortium was established. In all, six investigators have collaborated on fourteen separate STARR grants studying a broad spectrum of cancers and therapies.



HOPP faculty mingling at a Star Cancer Consortium event



### THE CANCER GENOME ATLAS PROJECT

The Cancer Genome Atlas (TCGA) is a comprehensive and coordinated effort to accelerate our understanding of the molecular basis of cancer through the application of genome analysis technologies, including large-scale genome sequencing. Funded by the National Cancer Institute, this endeavor has furthered the genetic knowledge of cancers and increased our understanding of possible therapeutic targets to fight cancers on a molecular level.

Dr. Timothy Chan, in conjunction with the Department of Surgery and Department of Pathology at Memorial Sloan-Kettering, has been awarded a grant through the TCGA program that hopes to further the genetic knowledge of colorectal cancers.



Although HOPP is still a fairly new program at MSKCC, its accomplishments in the past few years have contributed to the Center’s mission to further cancer research and treatment for patients. Our pace in achieving significant accomplishments is steady, and this year HOPP was able to make its mark in the world of news and media, as well as science.

## 2010 ACCOMPLISHMENTS

### GRANTS & FUNDING

| Applications          | 2010      |
|-----------------------|-----------|
| Federal Grants        | 30        |
| Industrial Agreements | 6         |
| Non-Fed Competitions  | 39        |
| Internal Competitions | 17        |
| <b>Total</b>          | <b>92</b> |

| Awards                | 2008      | 2009      | 2010      |
|-----------------------|-----------|-----------|-----------|
| Federal Grants        | 6         | 7         | 11        |
| Industrial Agreements | 4         | 2         | 5         |
| Non-Fed Competitions  | 8         | 11        | 21        |
| Internal Competitions | 6         | 7         | 11        |
| <b>Total</b>          | <b>29</b> | <b>28</b> | <b>53</b> |

### AWARDS & HONORS

In 2010, HOPP received a wide range of scientific awards and honors that support our mission to develop and deliver progressive translational cancer research.

The following awards and honors from the past year exemplify HOPP’s ability to be recognized for its contribution to the world of cancer research.

| Faculty          | Name   | Granted by  |
|------------------|--|---|
| Timothy Chan     | Distinguished Scientist                          | Sontag Foundation                                 |
| Cameron Brennan  | Kirby Award                                      | Kirby Foundation                                  |
|                  | Leon Levy Young Investigator                     | Leon Levy Foundation                              |
| Ross Levine      | Elected to Membership                            | American Society of Clinical Investigators (ASCI) |
| Ingo Mellinghoff | Leon Levy Neuroscience Fellow/Research Professor | Leon Levy Foundation                              |
| Charles Sawyers  | Elected to Membership                            | National Academy of Sciences                      |
| David Solit      | Elected to Membership                            | American Society of Clinical Investigators (ASCI) |

## MEDIA HIGHLIGHTS

### STAND UP TO CANCER

Dream Team Leader – Dr. Charles Sawyers

Stand Up to Cancer (SU2C) is a program that is working to fundraise for cancer research. Its mission states that it “is a new initiative created to accelerate groundbreaking cancer research that will get new therapies to patients quickly and save lives. SU2C’s goal is to bring together the best and the brightest in the cancer community, encouraging collaboration instead of competition. By galvanizing

the entertainment industry, SU2C creates awareness and builds broad public support for this effort.”

HOPP’s Chair, Dr. Charles Sawyers, is a Co-Leader of one of Stand Up to Cancer’s Dream Teams: Targeting PI3K in Women’s Cancers. See him at <http://www.standup2cancer.org>.



### ROCK STARS OF SCIENCE

2010 Rock Doc – Dr. Charles Sawyers

With the same concept as Stand Up to Cancer, Rock Stars of Science showcases the necessity of research funds in the fight toward the cure for cancer. Its mission is two-fold: 1) to hasten the cure for diseases like cancer, HIV/AIDS, and Alzheimer’s disease, and 2) to inspire the next generation to choose careers in science.



HOPP’s own Dr. Charles Sawyers represented HOPP in a photo shoot campaign with two other MSKCC “Stars” and Debbie Harry from the rock group Blondie. As part of the campaign, musical rock stars and scientific stars pose side by side in support for finding a cure to prove to the next generation that it is not only musicians who are stars, but also those who work toward helping human kind.

You can visit the RSOS website at [www.rockstarsofscience.org](http://www.rockstarsofscience.org).

View a video of Dr. Sawyers and the Geoffrey Beene “Stars” on his personal Rock Doc page: [http://www.rockstarsofscience.org/2010\\_rockdocs\\_sawyers.htm](http://www.rockstarsofscience.org/2010_rockdocs_sawyers.htm).

“The researcher who has one foot in the clinic and one foot in the lab leads a somewhat schizophrenic life at times. So first of all, it takes an incredibly dedicated individual because they have to go to school to become a doctor, and they also have to go to school to become a scientist and marry the two together. But once you have that combination of training, it is a very powerful set of skills that allows such a person to become the glue between two different forces that are both aligned to attacking cancer.”

– Dr. Charles Sawyers, from the Rock Stars of Science video

### AN EVENING WITH JAMES BLAKE

A Reception to Benefit the Thomas Blake Sr. Memorial Cancer Research Fund  
2010 Speaker – Dr. Ross Levine

On November 30, tennis star James Blake held his annual fundraiser—Serving for a Cure—to raise money for the Thomas Blake Sr. Memorial Research Fund at Memorial Sloan-Kettering Cancer Center. Named in memory of James’s father, the fund provides seed money for leading-edge science, with the goal of rapidly turning laboratory discoveries into better treatments for patients.

HOPP’s Dr. Ross Levine was asked to speak at the event. He emphasized the importance of supporting translational research and the critical role the Blake Fund plays in enabling the type of exciting science that is leading to new diagnostic and therapeutic strategies for cancer patients.

For more information, visit [http://www.jamesblaketennis.com/jb%20pages/10\\_memorial.htm](http://www.jamesblaketennis.com/jb%20pages/10_memorial.htm).



## FUNDRAISING VIDEOS ON YOUTUBE

Dr. Charles Sawyers

“Your Gift Goes Further” and “Together We Will Win”



Most organizations rely heavily on the generosity of philanthropists to sustain their efforts. HOPP, in an attempt to stay current and reach as many people as possible, has launched a video on the MSKCC YouTube site. You can view HOPP's Department Chair, Dr. Charles Sawyers, here as he and other doctors at MSKCC explain what donor dollars enable the institution to accomplish.

Find the video on the MSKCC's YouTube

site, <http://www.youtube.com/user/mskcc?blend=2&ob=video-mustangbase>.

## ONC LIVE – YOUR LINK TO EVERYTHING ONCOLOGY

Dr. Timothy Chan

Linking Parkinson's Disease and Cancer



Dr. Timothy Chan is one of the Sontag Foundation's Distinguished Scientist Awardees for 2010. In his research, Dr. Chan is studying a signaling pathway suspected to be involved in causing brain tumors to become highly aggressive.

Through these awards, the Sontag Foundation recognizes and supports the work of outstanding early career scientists whose research has the potential to generate new knowledge relating to causes, cures, or treatments of brain tumors. Each award combines career development components with a grant totaling \$600,000 to support the recipients' brain tumor research over a four-year period.

Sontag Foundation Website: [www.sontagfoundation.org](http://www.sontagfoundation.org)

## ABC NEWS

Dr. Marc Ladanyi

Cancer Genomics: Targeting Treatment to the Patient

During the Stand Up to Cancer campaign, ABC News Health published articles that spotlight the progress that certain cancer treatments have made. One of the articles was titled “Cancer Genomics Researchers Seek Individualized Cancer Treatment.” HOPP Member Dr. Marc Ladanyi was quoted in the article, which can be found on [www.ABCNews.com](http://www.ABCNews.com), explaining what personalized cancer therapy means to the patient and to the doctor:

*“This is the model of personalized cancer therapy,” says Dr. Marc Ladanyi, chief of the Molecular Diagnostics Service at Memorial Sloan-Kettering Cancer Center in New York. “We don't just look at [a tumor] under the microscope to see how aggressive it is; we also characterize which mutations are present in the cancer, so that from the get-go you know if your cancer can be treated with specific drugs.”*

At Sloan-Kettering, patients with non-small cell lung cancer — the most common form of the disease — have their cancer cells tested for over forty different mutations. Once a mutation is identified, doctors can suggest specific treatments based on the patient's cancer mutation.

Clinical trials are underway at the M.D. Anderson Center to determine the success rate of genetic tests, such as the ones performed at Memorial Sloan-Kettering, not only in lung cancer but in metastatic colorectal cancer as well.

## HOPP TRIUMPHS

### New Recruits:

1. Emily Cheng from Washington University | St. Louis, MO  
Clinical Department: Pathology
2. James Hsieh from Washington University | St. Louis, MO  
Clinical Department: Medicine, Genitourinary Oncology Service

- **Dr. David Solit and Ross Levine** both elected to American Society of Clinical Investigation (ASCI)
- **Dr. David Solit** awarded a multicenter grant from the Melanoma Research Foundation
- **Dr. Timothy Chan** was a 2010 Sontag Foundation Grant Recipient
- **MSKCC Prostate Genome Project published** integrative genomic profiling of human prostate cancer. Cancer Cell. 2010 (Taylor et al.)
- **Clinical trial results of a drug developed by a HOPP lab (the antiandrogen MDV3100) published** Antitumor activity of MDV3100 in castration-resistant prostate cancer: a phase I–II study. Lancet 2010 (Scher et al.)



The full article can be found at:  
[www.abcnews.com/Health/StandUp2Cancer](http://www.abcnews.com/Health/StandUp2Cancer)

DR. INGO MELLINGHOFF

“The goal is to increase the success of developing targeted therapies for brain cancer by testing promising drugs in the right patient population.”



Dr. Ingo Mellinghoff, Assistant Member, HOPP; Assistant Attending, Department of Neurology

*Dr. Ingo Mellinghoff is a well-respected glioblastoma researcher. In 2007, he joined HOPP and is currently part of a multi-institutional clinical trial consortium that is leading the way for clinical trials and translational research in brain tumors.*

Glioblastoma is a rare disease, and you need to collaborate with centers throughout the United States to capture a larger fraction of the disease pool. The centers participating in this clinical trial consortium are MKSCC, USCF, UCLA, Dana Farber, and Mass General.

The idea is for some of the biggest centers in brain cancer, clinical care, and research to molecularly profile the tumor tissue of more or less all their patients and deposit this information in a shared and de-identified database. Each tumor is sorted by its most prominent targetable genetic abnormality, and then patients will be enrolled accordingly in a clinical trial, which will be run jointly and in parallel at all these centers.

So, if two different patients have tumors with the same mutation in the same gene, they will be able to go on the same study even if one lives in Boston and the other in San Francisco. It will be based on the genetic abnormality of their tumor.

This is a unique effort to organize the molecular profiling of patient tumors between high volume centers, while making it actionable by linking it to the clinical trial agenda. The profiling here will be done jointly between Drs. Jason Huse, Cameron Brennan, the Brain Tumor Center, and my lab. We've spent the past two years developing all the necessary tools and reagents to test on paraffin-embedded tissues for signature abnormalities.

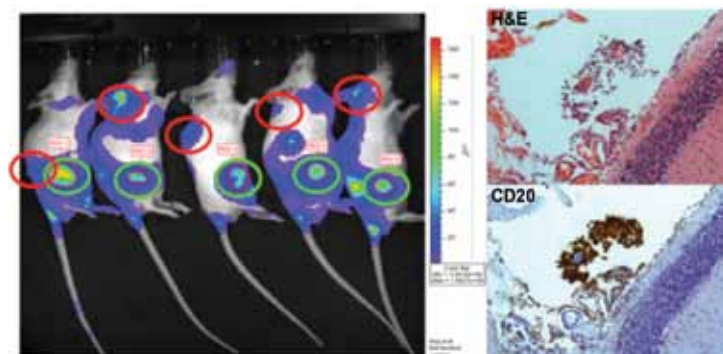
This information will be the basis for clinical trial enrollment at our center. I serve as a site PI for MSKCC. I, along with the other four PIs from the other institutions, get together once a month for a conference call to update one another on where we stand with the open group protocol.

This is a relatively new initiative, and the patient-de-identified tumor bank is now online as a shared Web tool. This is a departure from the usual clinical trial design in neurooncology and a stepping stone toward “personalized” cancer therapy for glioma.

During the last two years, we have spent substantial effort optimizing our molecular profiling assays to reliably identify signature alterations in glioma using paraffin-

embedded tumor samples. This groundwork was critical because many of our patients are referred from outside hospitals that currently lack the infrastructure for routine banking of frozen tumor tissue and hence will only be able to provide paraffin-embedded tissue as a source for our profiling.

We are excited about this progress as it provides the foundation for hypothesis-driven clinical trials and will fuel further projects in the laboratory. We are fortunate that the MSKCC Brain Tumor Center contributes critical resources to this effort and provides a forum for the frequent exchange of ideas between clinical and basic science investigators. We are meeting regularly to discuss new compounds, new concepts, and questions related to clinical trial design and prospective molecular screening of tumor samples. It is an exciting group effort which, we believe, will substantially accelerate the discovery of new treatments for our brain tumors.



(Left) Lymphoma cells metastasizing to the CNS after IV injection. Luciferase imaging identifies lymphoma cells in the bone marrow (green circles) and CNS (red circles). (Right) Histology (H&E) and immunohistochemistry (CD20) confirm metastatic cells in the CNS.



**Emily Cheng**, “*BID, BIM, and PUMA are Essential for Activation of the BAX- and BAK-Dependent Cell Death Program.*” *Science* 2010 Dec 3; 330(6009):1390–3.

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