



MASSACHUSETTS
GENERAL HOSPITAL

CANCER CENTER



Massachusetts General Hospital Cancer Center *Advancing cancer care through groundbreaking research*

Massachusetts General Hospital Cancer Center combines a commitment to further the most innovative scientific findings with a dedication to deliver the highest standard of patient care. A devoted body of investigators works hand in hand with caregivers to push the boundaries of discovery and speed findings into clinical advancements to impact cancer care. An emphasis on delivering compassionate care to each individual patient and family remains a hallmark of the Cancer Center. This approach has led *U.S. News & World Report* to recognize Mass General Cancer Center, year after year, among the top in the field in its “Best Hospitals” survey.

One of the Cancer Center’s distinguishing features is the Center for Cancer Research (CCR). The CCR’s 32 laboratory teams, each led by a preeminent principal investigator, are probing every facet of basic cancer research in fields from genetics and genomics to computational biology and stem cell science to advance knowledge aimed at preventing and curing cancer. Over the past year, the CCR’s scientists have published 93 peer-reviewed papers in leading scientific journals. These findings are shaping current cancer research practices and impacting future treatment protocols both at Mass General and around the world.

As this year marks Mass General’s bicentennial, the hospital has launched the Campaign for the Third Century of MGH Medicine. The Cancer Center is playing a prominent role in this \$1.5 billion fundraising campaign, targeting a \$350 million goal, to help ensure that the hospital’s mission is secure well into its third century. Funds raised for the Cancer Center will fuel five Thematic Priorities which cut across each of the center’s 20 disease specific programs and sub-specialties; these priorities were established by Cancer Center leadership and represent the Cancer Center’s vision and strategic approach to cancer research and care. This report highlights novel examples of how Cancer Center physicians and scientists have made progress toward these priorities over the past year.

Discovering the fundamental causes of cancer as a guide to prevention, early detection and treatment

At the most basic scientific level, Cancer Center investigators are working to determine the underpinnings of human cancers. Recent advances are allowing researchers to gain a deeper understanding of the genetic makeup of cancers, which is leading to the development of personalized therapy approaches at earlier points in the treatment cycle.

Miguel Rivera, MD, Bradley Bernstein, MD, PhD, and Daniel Haber, MD, PhD, at the Center for Cancer Research and several colleagues in the field conducted an investigation of Wilms tumor, the most common pediatric kidney cancer. Building on Dr. Bernstein's earlier work which showed that chromatin, a part of chromosomes that packages DNA, played an important role in cell developmental processes, Drs. Bernstein, Haber and Rivera compared Wilms tumor cells, embryonic stem cells and normal kidney cells to determine if there were chromatin factors which contributed to the onset of this disease. As published in the June 4 edition of *Cell Stem Cell*, they found that the chromatin configuration of Wilms tumor cells is similar to that of embryonic stem cells and these similarities may contribute to the development of Wilms tumors and potentially other pediatric cancers.

Konrad Hochedlinger, PhD, and Toshihiro Shioda, MD, PhD, led an important study to determine if induced pluripotent stem cells (iPSCs) and mammalian derived embryonic stem cells are equivalent. iPSCs are adult cells which have been genetically reprogrammed to an embryonic stem cell-like state, and as such, do not have the ethical concerns of embryonic stem cells. Previous work had shown major differences in the cells' basic makeup. In a novel paper published in the May 13 issue of *Nature*, Drs. Hochedlinger and Shioda describe that genetically matched embryonic stem cells and iPSCs are indistinguishable with the exception of a single gene group. This finding holds great potential for the use and utility of iPSCs in the future and will lead to improved cell reprogramming strategies.

Shiv Pillai, MD, PhD, and several colleagues at the CCR examined the role of a gene encoding the enzyme, sialic acid acetyltransferase, which controls signaling by the immune system's B-cells. B-cells are a type of white blood cell; when disregulated by the functional absence of this enzyme, B-cells can contribute to the onset of specific autoimmune disorders. Dr. Pillai's laboratory found that individuals who harbor this gene mutation had a significantly higher chance of having an autoimmune disease, like rheumatoid arthritis and type 1 diabetes. Dr. Pillai's findings were published in the June 16 edition of *Nature*. Moreover, as the pathways that cause these diseases are linked to the development of certain cancers, like lymphomas, Dr. Pillai is studying these pathways as a means to develop novel therapies.





Targeting early cancers through precision surgery and focused radiation

Less invasive and more precise approaches to treating cancers while a tumor is still in its primary site are essential to improving outcomes for patients. Proton therapy, focused ultrasound, minimally invasive surgery and advanced imaging are a few of the approaches available to target tumors in a localized area and to increase the possibility of treatment success.

Thomas DeLaney, MD, and several colleagues completed a trial to identify the most effective treatment for patients with retroperitoneum sarcomas. Retroperitoneum sarcomas are rare tumors typically manifesting in the abdomen, and the standard treatment is surgical removal of the tumor and surrounding organs. The goal of Dr. DeLaney's study was to reduce local recurrence of the disease utilizing the combination of preoperative proton-beam therapy and surgical resection of the tumor with intraoperative electron radiation therapy. This approach, as detailed in the February 12, 2010 edition of the *Annals of Surgical Oncology*, is more targeted to the tumor and surrounding tissues. Nearly three years after the procedure, the local tumor reoccurrence rates were significantly lower than the standard treatment. Additional investigations into the role of chemotherapy and targeted drugs are on the horizon to further improve treatment results.

Rakesh Jain, PhD, completed a study to determine how acute radiation syndrome, exposure to very high doses of ionizing radiation, causes troublesome and sometimes deadly damage to the gastrointestinal tract – called GI syndrome. Through the years, many different theories have emerged, however the underlying cause of radiation-induced GI syndrome has not been confirmed, and currently, there are not any approved therapies or treatments for this condition. Dr. Jain's investigation focused on the p53 gene, which is a gene known to stop the formation of tumors. He found that by selectively removing p53 from the outside of the gastrointestinal tract, the tissues were protected from GI syndrome after radiation. These findings are especially promising for individuals with cancer who experience difficulty tolerating the late effects from radiation therapy. Dr. Jain's findings were published in the January 29, 2010 issue of *Science*.

Targeting complex and advanced cancers through smart drugs

Human cancers vary significantly in their genetic makeup and an extensive array of drugs has been used to treat patients with varying results. By studying the genetic and genomic properties of cancers, investigators are applying the most appropriate “smart drugs” to guide treatment decisions.

Metastatic melanoma is a severe and fast spreading form of cancer. For the past several years, **Keith Flaherty, MD**, has been leading a multicenter clinical trial of a targeted smart drug, PLX4032, for the treatment of metastatic melanoma in patients who harbor the B-RAF genetic mutation. The B-RAF mutation accounts for nearly 60% of all melanomas. Dr. Flaherty’s findings, which were published in the August 26 issue of *The New England Journal of Medicine*, showed that the vast majority of patients with this genetic mutation who were treated with this targeted therapy experienced complete or partial tumor regression – a dramatic step forward in the treatment of this disease. In 2010, *The New York Times* published a three part series chronicling the long and challenging road Dr. Flaherty has traveled to bring this important discovery to light. Dr. Flaherty is currently leading a phase III study to show how the drug affects patients’ long term survival – the results could represent a paradigm shift for patients with melanoma.

Eunice Kwak, MD, PhD, led an international clinical trial to test the safety and effectiveness of a targeted oral drug aimed at patients with non-small cell lung cancer whose genes harbor EML4 and anaplastic lymphoma kinase (ALK). EML4 and ALK are proteins which can lead to development of tumors, and account for a very small portion of patients with non-small cell lung cancer. Of significant note, Dr. Kwak found that patients with this particular type of cancer tended to be younger and had little, if any, exposure to tobacco products. Moreover, many of these patients had already been treated unsuccessfully with conventional therapies. As reported in the October 28 issue of *The New England Journal of Medicine*, Dr. Kwak found that the majority of patients treated with this targeted drug experienced tumor shrinkage or stabilization of the disease.

Immune thrombocytopenia is a blood disorder which is characterized by abnormally low platelet counts in the bloodstream. Platelets are a type of blood cell which are necessary for clotting. This disorder can be a signal for more serious medical conditions, including cancers. **David Kuter, MD**, completed an international, multicenter trial to evaluate the effects of a targeted drug, romiplostim, versus the standard treatment protocol. The typical standard of care for patients with this disease consists of medical therapies, and often surgery, to remove all or part of the spleen. Dr. Kuter found that patients treated with this agent had less bleeding, increased and sustained platelet counts, a lower need for a surgical intervention and an improved quality of life compared with patients treated with the standard protocol. Dr. Kuter's findings were published in the November 11 edition of *The New England Journal of Medicine*.





Accelerating the delivery of research discoveries to people with cancer

Managing and overseeing the initiation and development of clinician-directed and sponsored trials is critical to ensuring successful transition of research findings from the laboratory bench to the bedside. To better address the unique issues clinical investigators face and increased regulatory demands, the Cancer Center established a Protocol Office to transform scientific discoveries into powerful new treatments.

A. John Iafrate, MD, PhD, and Leif Ellisen, MD, PhD, co-direct the Translational Research Laboratory, and along with their colleagues, they are leading the Cancer Center's effort to analyze the genetic makeup of each patient's tumor for cancer-causing mutations. Through an automated process, Dr. Iafrate, Dr. Ellisen and their colleagues are identifying the unique characteristics of tumors and matching them with the most appropriate targeted therapy. **Dr. Iafrate and Long Phi Le, MD, PhD**, were the recipients of the **Dr. James Watson Healthcare Grant** by Ion Torrent. The award is named in honor of Dr. Watson who co-discovered the DNA helix structure. Drs. Iafrate and Le's aim is to develop and study a broad based genotype analysis of key genetic targets for clinically relevant information to guide treatment decisions. As part of the award, they are testing a gene sequencing device made by Ion Torrent for its ability to perform this analysis, which is used in addition to other existing sequencing platforms in the Cancer Center.



Treating the patient, supporting the family and educating the community

Improving the physical, emotional and spiritual health of patients and families affected by a cancer diagnosis is central to the Cancer Center's mission. By offering a wealth of support services, patients and their loved ones can access valuable resources and information, attend wellness workshops and counseling groups and get guidance on informing children of cancer diagnosis.

Non-small cell lung cancer is the most common type of lung cancer, and in many instances by the time of diagnosis, the cancer has already spread to other areas of the body – limiting treatment options and shortening survival outcomes. **Jennifer Temel, MD**, completed an innovative study at Mass General to examine the effects of incorporating palliative care, along with routine oncologic care, shortly after diagnosis of metastatic non-small cell lung cancer. Palliative care, consisting of a multidisciplinary team of physicians, nurses, social workers and other caregivers, is typically initiated late in the disease course. Dr. Temel found that patients who received palliative care early in the treatment cycle experienced significant improvement in mood and overall quality of life, and additionally, lived longer than patients who received standard oncologic care alone. Dr. Temel's findings were published in the August 19 edition of *The New England Journal of Medicine*, and will likely lead to a change in the way these important support services are provided in the future.

Inga Lennes, MD, leads the new Survivorship Program. Dr. Lennes along with **Elizabeth Davis, MD**, and their colleagues work in collaboration with primary care providers to address important health and well-being issues for patients who have completed their treatment protocols. By combining health and wellness information with existing survivor services provided through the Maxwell V. Blum Cancer Resource Room and the HOPES Program, patients have a wealth of resources to assist with all facets of long-term care. Moreover, this May the Cancer Center, in coordination with the Network for Patients and Families Program, hosted the **Celebrating Cancer Survivorship** conference. This day long symposium consisted of informational programs, supportive workshops and a wellness fair to provide vital information and assistance to individuals and families living with the day-to-day and long-term realities of a cancer diagnosis. Plans are underway for next year's conference, to be held in April 2011.



Cancer Center Leadership Highlights

In 2010, 22 new clinicians joined the Cancer Center's staff, along with three new researchers at the Center for Cancer Research. Provided, in the sidebar, is a full listing of these individuals and their specialties:

Jose ´ Baselga, MD, PhD, joined Mass General in July as the chief of Hematology Oncology and associate director of the Cancer Center. Dr. Baselga is a world renowned leader in clinical cancer research and an authority in developing targeted therapies for breast cancer. He is on the editorial boards of several leading scientific journals, and has published more than 250 peer-reviewed articles and more than 400 abstracts and book chapters. Previously, he served as chairman of the Medical Oncology Service at the Vall d'Hebron University Hospital in Barcelona and was the founding director of Vall d'Hebron Institute of Oncology. Dr. Baselga succeeds Thomas Lynch, MD, who left the Cancer Center last year to serve as director of Yale Cancer Center in New Haven.

In April, after 15 years of dedicated service, **Bruce Chabner, MD**, stepped down as Clinical Director of the Cancer Center. Under Dr. Chabner's leadership, the Cancer Center's clinical volume and research infrastructure grew dramatically and its stature and prominence in the medical community rose both locally and nationally.

David Ryan, MD, has assumed the positions of Clinical Director of the Cancer Center and Associate Chief of the Division of Hematology/Oncology. Dr. Ryan is a highly respected caregiver and a leading investigator focusing on gastrointestinal cancers. For the past seven years, he has served as clinical director of the Tucker Gosnell Center for Gastrointestinal Cancers and he will continue to serve in this capacity.

Mo Motamedi, PhD, will join Mass General this spring as an assistant professor of medicine and serve in the Center for Cancer Research. Dr. Motamedi's research focuses on epigenetics – the study of changes in genes – and its role in basic cellular processes. Most notably, he has elucidated some of the most fundamental mechanisms of gene silencing. He is also studying chromatin and how different factors impact cell functions. Dr. Motamedi comes to Mass General from Harvard Medical School, where he serves as an investigator and an instructor in Cell Biology.

MEDICAL ONCOLOGY

Chief – Jose ´ Baselga, MD, PhD
Bone Marrow Transplant, Leukemia
Amir Fathi, MD

Breast Cancer

Michaela Higgins, MB, BCH

Gastrointestinal Cancers

David Ting, MD

Genitourinary Cancers

Philip Saylor, MD

Hematology

Annemarie Fogerty, MD

Hematology (Benign)

Katayoon Goodarzi, MD

Lymphoma

Jeffrey Barnes, MD, PhD

Pediatrics

Jessica Sachs, MD

Psychiatric Oncology (Survivorship)

Elizabeth Davis, MD

RADIATION ONCOLOGY

Gastrointestinal Cancers

Jennifer Wo, MD

Breast Cancer, Lymphoma

Karen Winkfield, MD, PhD

SURGERY/SURGICAL ONCOLOGY

Endocrine Tumors

Carrie Lubitz, MD

Gastrointestinal Cancers, Sarcoma

Sam Yoon, MD

Gynecologic Cancers

Whitfield Growdon, MD

Pediatric Neurosurgery

Ann-Christine Duhaime, MD

Thoracic Cancers

Ashok Muniappan, MD

PATHOLOGY

Bone Marrow Transplant, Lymphoma, Leukemia

Abner Louissaint, MD, PhD

Translational Research

Long Phi Le, MD, PhD

PALLIATIVE CARE

Kathleen Doyle, MD

Mihir Kamdar, MD

Lorie Smith, MD

CCR INVESTIGATORS

Cyril Benes, PhD

Mo Motamedi, PhD

Miguel Rivera, MD

Awards

National Institutes of Health Director's Pioneer Award

J. Keith Joung, MD, PhD, in the Massachusetts General Hospital Center for Cancer Research and the Center for Computational and Integrative Biology, received the National Institutes of Health Director's Pioneer Award. This award recognizes scientists who propose highly innovative approaches to major challenges in biomedical and behavioral research. Dr. Joung's research focuses on developing new ways of reprogramming skin cells into stem cell like states, and he is one of 17 individuals who received this year's award.

Initiatives



June marked the Cancer Center's third annual **one hundred** dinner. The late Senator Edward Kennedy was among the 100 individuals and groups honored for their commitment to advancing the fight against cancer, and Senator Kennedy's son, Ted Kennedy, Jr., provided the keynote address. Since **the one hundred's** founding, more than \$1.5 million has been raised through this event to support the Cancer Center's research, education, patient care and community outreach initiatives.

The Massachusetts General Hospital Center for Lymphoma is well known for providing exceptional clinical outcomes to patients with lymphoma. **Jon and Jo Ann Hagler** have generously supported the establishment of two endowed chairs – in hematology-oncology and hematologic malignancies – at Mass General, and an endowed research fund to advance the Center for Lymphoma's work.

In September, **Stand Up To Cancer** (SU2C) held its second network television fundraiser. The telethon brought together the entertainment community and members of the 5 "Dream Teams," previously funded by SU2C, in order to highlight each of the teams' innovative projects aimed at eradicating cancer. Last year, the "Dream Team" at Mass General Cancer Center received a \$15 million grant from SU2C to advance the circulating tumor cell (CTC) technology. **Daniel Haber, MD, PhD**, and **Mehmet Toner, PhD**, are leading the "Dream Team" in collaboration with members from four other institutions; the CTC-chip was originally developed at Mass General in 2007.



Building on the success and promise of the **CTC-chip**, in January, the Cancer Center announced a unique partnership with the current commercial CTC manufacturer, Johnson & Johnson. Based on the specialized skills of the Mass General team, Johnson & Johnson has committed to building a center for excellence in CTC technology at Mass General, and will partner with MGH scientists and engineers to develop the next generation of devices that could be broadly available to clinicians everywhere.



Initiatives (cont.)



In November, the hospital celebrated the establishment of the **Bruce A. Chabner Chair in Hematology Oncology** at Mass General. This philanthropically supported endowed chair recognizes **Dr. Chabner's** significant achievements in research and clinical care, and **Dr. Baselga** was appointed as the inaugural incumbent. The Chabner Chair is the Cancer Center's first endowed chair based solely at Mass General.



Mass General, Brigham and Women's and Dana-Farber have teamed up with the New England Patriots to **Kick Cancer**, a program aimed at increasing cancer awareness among Patriots fans. This season, at every home game, fans received valuable information on cancer screening and prevention techniques; each of the Patriots' home games focused on a different type of cancer, and on December 6, Mass General helped the Patriots promote colon cancer awareness.