Massachusetts General Hospital Cancer Center offers an exceptional level of expertise in 24 clinical programs and a vast array of support and educational services. A synergy between caregivers in the clinics and researchers in the laboratories ensures that individuals receive the most scientifically advanced, personalized care throughout their hospital experience. The Cancer Center’s multidisciplinary and compassionate approach has led *US News & World Report* to rank the center, once again, as one of the finest cancer centers in the nation. The magazine also named Mass General as the nation’s #1 hospital.

To ensure a bright future for the hospital and its patients, Mass General is in the final year of the *Campaign for the Third Century of MGH Medicine*, which seeks to raise $1.5 billion. The Cancer Center is playing a prominent role in the success of this campaign. Generous philanthropic support from loyal donors helps make the Cancer Center’s important work possible. This report highlights the Cancer Center’s comprehensive approach to conquering cancer, and it presents important updates and announcements from the Cancer Center in 2012.
Mass General has been a leader in the development of microfluidics-based devices for capturing, imaging, and analyzing rare circulating tumor cells (CTCs).

**In the Laboratory**

Mass General has been a leader in the development of microfluidics-based devices for capturing, imaging, and analyzing rare circulating tumor cells (CTCs) from the blood of patients with metastatic disease. Daniel A. Haber, MD, PhD, Mehmet Toner, PhD, and a team of physicians, basic scientists, and engineers conducted an exploratory study to determine whether tracking androgen receptor signaling in CTCs from patients with metastatic prostate cancer could help guide therapy.

Most patients with metastatic prostate cancer initially respond well to androgen deprivation therapy, but eventually their tumors become resistant to first-line drugs and their cancer progresses. Dr. Haber and colleagues showed that measuring pre- and post-treatment androgen receptor signaling within captured CTCs – using the Evans Assay – may provide a new biomarker for metastatic prostate cancer and help identify patients most likely to respond to second-line therapies.¹

CTCs also play an important role in research about pancreatic cancer, one of the deadliest cancers. Using CTC technology and RNA sequencing, Dr. Haber and colleagues identified Wnt2 as a candidate gene enriched in CTCs. In mouse and human models, Dr. Haber’s findings indicate that Wnt signaling pathways may contribute to development of pancreatic cancer, and they may lead to identification of a novel drug target to suppress metastasis.²

Konrad Hochedlinger, PhD, leads a laboratory focused on the development of induced pluripotent stem cells (iPSCs). iPSCs can be derived from any patient’s skin or blood cells and can be reprogrammed to an embryonic stem cell-like state that makes them capable of developing into all tissues of the body. Prior studies have shown, however, that iPSCs may not have the same regenerative potential as stem cells derived from mammalian embryonic cells due to certain genetic and other abnormalities that disrupt the reprogramming process. Dr. Hochedlinger previously discovered that a common abnormality in mouse iPSCs is faulty regulation of a gene cluster, Dlk1-Dio3. In 2012 Dr. Hochedlinger and colleagues showed that adding ascorbic acid to the reprogramming culture can prevent aberrant regulation of this cluster, showing for the first time that a small compound can greatly improve the quality and potential of mammalian iPSCs, equal to the developmental potential of embryonic stem cells.³ This work will ultimately inform the development of new strategies to treat cancer.

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Center for Cancer Research

The Center for Cancer Research (CCR) serves as the engine of discovery for the Cancer Center. The CCR consists of 36 laboratories and more than 300 researchers whose interests cover the spectrum of cancer research. In 2012, CCR scientists published more than 220 peer-reviewed papers and made significant progress in advancing our understanding of cancer biology.

In 2013, the CCR’s goals are to advance our understanding of fundamental biological processes disrupted in cancer, develop new diagnostic and therapeutic tools that can alter the course of the disease at its earliest stages, and improve clinical outcomes for patients treated at Mass General and around the world.
Metastatic melanoma is aggressive and fast-spreading. In patients whose metastases harbor certain mutations in the BRAF gene, targeted therapies can be effective, but resistance to monotherapy typically occurs in less than one year. Keith Flaherty, MD, led a multi-center clinical trial looking at silencing an intracellular signaling pathway with a combination of therapies. These drugs target two links in the pathway, the proteins BRAF and MEK. The trial showed that by combining dabrafenib, a BRAF inhibitor, with trametinib, a MEK inhibitor, patients achieved longer progression-free survival as well as greater tumor regression rates compared with patients receiving dabrafenib monotherapy. On the basis of these promising findings, two phase 3 trials have been initiated.

Alice Shaw, MD, led a study to investigate the role played by ROS1, a receptor tyrosine kinase gene, in patients with non-small-cell lung cancer (NSCLC). Little has been known about this gene and no agents targeting its product have been available. Dr. Shaw and colleagues previously found that the drug crizotinib was highly effective in treating NSCLC patients with chromosomal rearrangements of another gene, ALK. Studies like these have highlighted the need to match targeted therapies to genetically defined patient populations. Dr. Shaw found that approximately 2% of patients with NSCLC harbor ROS1 chromosomal rearrangements, and that the clinical profile of these patients resembles that of patients with ALK rearrangement, including being young at the time of disease onset and being nonsmokers. Moreover, her research indicated that crizotinib is effective in the treatment of ROS1-positive tumors.

Studies like these have highlighted the need to match targeted therapies to genetically defined patient populations.
The Henri and Belinda Termeer Center for Targeted Therapies

In December, the Cancer Center formally opened The Henri and Belinda Termeer Center for Targeted Therapies. Located in a newly renovated suite on the seventh floor of the Yawkey Center for Outpatient Care, the Termeer Center aims to improve patients’ access to novel targeted cancer therapies through clinical trials. Dr. Flaherty, a melanoma specialist and internationally renowned leader in targeted therapies, has been named director of the Termeer Center.

The Cancer Center held a symposium and reception in October to celebrate the opening of the Termeer Center and acknowledge the generosity of Henri and Belinda Termeer for their gift that made the center possible. The symposium was held in Mass General’s Ether Dome, which recognizes the hospital’s storied past with the first use of ether and represents the future in developing personalized therapies. The symposium was hosted by Daniel A. Haber, MD, PhD, and featured presentations by Robert Weinberg, PhD, of MIT; José Baselga, MD, PhD; Jeff Engelman, MD, PhD; and Dr. Flaherty.

To view the symposium, please visit:

www.massgeneral.org/targetedtherapy (on Multimedia tab)

*Pictured above: Cutting the ceremonial ribbon on October 2 are (L-R) Dr. Peter Slavin, Dr. Daniel Haber, John Murphy, Adriana Termeer, Belinda Termeer, Henri Termeer, Dr. Keith Flaherty.*
Focused Radiation

Jason Efstathiou, MD, PhD, is leading a phase 3 trial to compare the clinical effectiveness of proton beam therapy and intensity-modulated radiotherapy in patients with early-stage prostate cancer. Both approaches provide targeted, high doses of radiation, while minimizing toxicity to surrounding tissues. However, proton beam therapy is substantially more expensive. To date, no definitive study has demonstrated which technique is more beneficial or more cost-effective for patients with prostate cancer. Dr. Efstathiou seeks to generate evidence that will help guide such treatment decisions.

Osteosarcoma is a type of bone cancer that most commonly affects patients in their 20s. Local tumor control through surgery is often the most effective treatment, but sometimes surgery is difficult or impossible. Thomas DeLaney, MD, and a multidisciplinary team conducted a retrospective study showing that proton-based radiotherapy allows locally curative treatment for some patients whose osteosarcoma cannot be treated through surgical removal of the tumor.6 Radiation therapy is important treatment for many patients with brain tumors, but it can cause long-term health issues, such as cognitive defects and hearing loss, especially in children. Karen Kuhlthau, PhD, and colleagues conducted a first-of-its-kind investigation to better understand how proton radiotherapy affects the health-related quality of life (HRQoL) of pediatric patients with brain tumors and the impact on their parents. Dr. Kuhlthau found that HRQoL scores for patients at the beginning of treatment were low, but after three years of follow-up, the scores approached those of healthy children.7 Dr. Kuhlthau hypothesizes that integration of mental health professionals into the treatment plan will further improve patients’ HRQoL.

Both approaches provide targeted, high doses of radiation, while minimizing toxicity to surrounding tissues.

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Milestones

As demands for proton therapy have increased, the Massachusetts Department of Public Health unanimously approved the application for a second proton machine at Mass General. The hospital will be the first in the country to have two proton accelerators, enabling more patients to receive potentially life-saving therapy and allowing investigators to conduct critical clinical research.

Mass General pioneered the use of proton therapy in 1962. Proton therapy enables clinicians to more precisely localize the radiation dosage when compared with other types of external beam radiotherapy, sparing nearby healthy tissue. This approach has proved to be highly effective in treating pediatric cancers such as a highly malignant primary brain tumor (medulloblastoma) as well as sarcomas and other cancers where surgical options are limited.

In September, Mass General celebrated the 10-year anniversary of its dedicated proton therapy center, the Francis H. Burr Proton Therapy Center. More than 5,500 patients have received treatment at the center since its inception, and its staff delivers more than 14,000 treatments annually.

For more information on the Cancer Center’s second proton machine, please visit:

massgeneral.org/protonexpansionvideo

Pictured above: Dr. Tracy Batchelor, Dr. Nancy Tarbell, Dr. Peter Slavin, Mr. Andrew Gordon, Mrs. Victoria Kennedy and Dr. Jay Loeffler at the 10th Anniversary event on September 20.
The incidence of hepatocellular carcinoma (HCC) – the most common type of liver cancer and the most common cause of cancer-related deaths worldwide – is rapidly increasing in the U.S. Few treatment options are available for the disease; surgery can be successful when the cancer is diagnosed early, but typically only 10% to 20% of patients are candidates for surgery. In a novel study, Kenneth Tanabe, MD, and Bryan Fuchs, PhD, examined the role that epidermal growth factor (EGF), which stimulates cell production, plays in HCC and cirrhosis. They found that erlotinib, which inhibits the EGF receptor (EGFR), prevents progression of cirrhosis and blocks development of HCC, and may reverse aspects of the disease. This could represent a new use for erlotinib and other EGFR inhibitors.

Patricia Sylla, MD, has completed a phase 1 clinical trial of trans-anal rectosigmoid resection for rectal carcinoma. Because this technique uses the body’s orifices to gain access to cancerous sites, it’s less invasive than typical laparoscopic surgery, sparing patients painful abdominal incisions. Based on the phase 1 trial, in which excellent oncologic outcomes with prompt recovery were seen, a larger phase 2 clinical trial is being conducted.

Michael Lanuti, MD, and Harald Ott, MD, in the Division of Thoracic Surgery at Mass General are world leaders in organ engineering. Drs. Lanuti and Ott pioneered novel developments in the use of cryopreserved aortic homograft to repair tracheal defects or partial laryngectomy defects related to cancer; this innovative reconstructive option permits preservation of airway, swallowing, and voice. Organ engineering also involves decellularization of whole organs to be used as scaffolds for engraftment of specialized cells to form viable and functional organs (e.g., heart, lung, kidney, pancreas) that could be transplanted and function in vivo. It has the potential for replacing organs (e.g., trachea, lung) in patients with cancer that would otherwise be untreatable.

Because this technique uses the body’s orifices to gain access to cancerous sites, it’s less invasive than typical laparoscopic surgery, sparing patients painful abdominal incisions.
Theresa McDonnell, ACNP-BC, is the new clinical director of the HOPES Program, which was developed in 1998 to bring integrated therapies to Cancer Center patients. Research has shown that integration of complementary therapies improves outcomes for patients and reduces healthcare costs. Over the next year, the program plans to expand programming and seek new opportunities to improve the patient experience at the Cancer Center.

Handling about 21,000 telephone inquiries each month, the MGH Cancer Center Call Center is a portal for patients, referring physicians, and individuals seeking information or care in the Cancer Center. To improve patient access to clinical expertise, the Call Center has added nursing staff to help triage calls and provide advice in urgent situations. As a result, the center has seen improvement in the time to intervention for the sickest patients seeking advice.

The Cancer Center has launched a collaborative effort between the Ambulatory Clinic Nursing and Patient Financial Services Teams, the Financial Care Coordination Project, to address patients’ concerns about health insurance coverage and payments. This initiative unites a disease subspecialty-trained nurse with an administrative care coordinator, forming a team that handles screening and prior authorizations, or in some cases, refers patients for financial counseling. This coordinated approach ensures that patients are free from worries regarding financial burdens, allowing them to concentrate on what’s most important – their health and well-being.
Focus on Survivorship

The Mass General Cancer Center held its annual Survivorship Conference in April. Called *Cancer in the Family – Living with Uncertainty*, the conference was sponsored by the Conquer Cancer Coalition of Massachusetts. It brought together individuals touched by cancer and their loved ones for an informative wide-ranging discussion. The initiative is part of the Cancer Center’s Survivorship Program, directed by Inga Lennes, MD. It is organized by the Network for Patients and Families, a volunteer peer support program based in the Maxwell V. Blum Cancer Resource Room.

The 2013 Survivorship Conference will be held on June 29. Call 617.724.1822 for more information.

Pictured above: Panelists (L-R), Susan Zuker, Kelly Haughey, Kurt Losert, Maggie Carvan, share their stories and perspectives on *Cancer in the Family: Living with Uncertainty*.
LEADERSHIP UPDATES

Nick Dyson, PhD, was appointed scientific director of the Mass General Cancer Center in February. Since joining the center 20 years ago, Dr. Dyson has established himself as an international leader in the study of cell cycle regulation. His findings have the potential to guide the design of novel, genetically focused therapies for many cancers. In his new role, Dr. Dyson will oversee laboratory investigators within the Center for Cancer Research and help shape the scientific vision of the Cancer Center. He succeeds Jeffrey Settleman, PhD, who left Mass General two years ago to lead oncology discovery at Genentech.

Michael Blute, MD, was appointed chief of Urology at Mass General in April, succeeding W. Scott McDougal, MD, who led the department since 1991. Dr. Blute’s major areas of interest include prostate cancer, nephron-sparing surgery for kidney masses, and management of complex renal cell and bladder neoplasms. He previously was chairman of the Department of Urology at the Mayo Clinic Cancer Center and interim chief of Urology and director of the Cancer Center of Excellence at the University of Massachusetts Memorial Medical Center.

In October, David Ryan, MD, became chief of the Division of Hematology/Oncology. Dr. Ryan, who began his career at Mass General in 1998, also serves as clinical director of the Cancer Center, overseeing 24 multidisciplinary disease centers and programs. He will also continue as clinical director of the Tucker Gosnell Center for Gastrointestinal Cancers.

Keith Flaherty, MD, was named director of the Henri and Belinda Termeer Center for Targeted Therapies in October. An internationally acclaimed clinical leader in targeted therapies for melanoma, Dr. Flaherty has expanded both basic knowledge of and patient access to breakthrough targeted therapies. As director of the Termeer Center, Dr. Flaherty will oversee a dedicated “first in human” phase 1 clinical facility.

Jeff Engelman, MD, PhD, was appointed director of the Molecular Therapeutics Program in October. He is a leading authority on thoracic cancers and has built an innovative laboratory and translational research program focusing on lung cancer and the mechanisms underlying drug sensitivity and resistance. Dr. Engelman will also serve as scientific director of the Termeer Center for Targeted Therapies to enhance drug discovery and accelerate early-phase drug trials.

Lee Zou, PhD, became (associate scientific) director of the Cancer Center in October. Dr. Zou began his career at Mass General as a researcher in the Center for Cancer Research. Recognized as a leader in the field of DNA damage signaling, he recently received an MGH Research Scholar Award, given to the most promising investigators at the hospital. This new appointment continues Dr. Zou’s leadership role within the Cancer Center, where he will work with Scientific Director Nick Dyson, PhD, and oversee educational programs and career development opportunities for faculty, fellows, and graduate students.
In November, Gad Getz, PhD, joined Mass General as an associate professor and director of Bioinformatics at the Cancer Center and MGH Department of Pathology. Dr. Getz is an internationally acclaimed leader in cancer genome analysis. He founded the cancer genome computational analysis group at the Broad Institute. In his new role, Dr. Getz will lead a collaborative effort within the Mass General Cancer Center and MGH Pathology to further develop and apply statistical methods to identify mutations in genes involved in tumor formation, and in treatment sensitivity and resistance.

Ann Prestipino, senior Vice President for Surgical and Anesthesia Services and Clinical Business Development, succeeded Sally Mason Boemer, Chief Financial Officer, as the senior Vice President for the Mass General Cancer Center in December. Ms. Prestipino, who was instrumental in the creation of the Cancer Center 25 years ago, has played a leading role at both Mass General and Partners HealthCare in the design and support of disease-centered service lines and is leading the MGH-wide strategic planning initiative.

José Baselga, MD, PhD, who joined Mass General in 2010 as chief of the Division of Hematology/Oncology and associate director of the Cancer Center, was named physician-in-chief of Memorial Sloan-Kettering Cancer Center in September. During his tenure at Mass General, Dr. Baselga led several high-profile clinical trials of targeted therapies for breast cancer.

### New Physicians

In 2012, 17 new physicians joined the Mass General Cancer Center staff:

**Diagnostic Radiology**
- Sheela Agarwal MD
- Hillary Kelly, MD
- Arun Krishnaraj, MD
- Frank Simeone, MD

**Medical Oncology**
- Jerry Azzoli, MD (Thoracic Oncology)
- Priscilla Brastianos, MD (Neuro-Oncology)
- Gregory Cote, MD, PhD (Sarcoma; Termeer Center)
- Don Dizon, MD (Gynecologic Oncology)
- Dejan Juric, MD (Breast Cancer; Termeer Center)

**Pathology**
- Amy Ly, MD (Breast Pathology)

**Psychiatric Oncology**
- Kelly Irwin, MD

**Radiation Oncology**
- Karen Bernstein, MD
- Timur Mitin, MD

**Surgery**
- James Becker, MD (Gastrointestinal Surgery)
- Michael Blute, MD (Urology)
- Dickin Ko, MD (Transplant Surgery)
- Brian Nahed, MD (Neurosurgery)
Endowed Chair Appointments

In October, the hospital celebrated the recently established James Howard Means, MD, Endowed Chair and its first incumbent, Gilbert H. Daniels, MD, co-director of the MGH Thyroid Clinic, medical director of the MGH Endocrine Tumor Center and co-director of the MGH Endocrine Tumor Genetics Clinic. Dr. Means served as the first chief of the MGH Thyroid Clinic – the hospital’s first specialty unit – until his retirement in 1951. Following Dr. Daniels’ retirement, the chair will be renamed the Gilbert H. Daniels, MD, Endowed Chair.

In November, the Cancer Center celebrated the establishment of the John R. Gallagher III and Katherine A. Gallagher Endowed Chair in Gastrointestinal Cancer Research. The inaugural incumbent is Nabeel Bardeesy, PhD, an internationally recognized leader in gastrointestinal cancers, particularly pancreatic and liver cancers. The chair was established through the generosity of John and Katherine Gallagher in honor of the care provided by Andrew Warshaw, MD, and David Ryan, MD.

The Rita M. Kelley Endowed Chair in Oncology has been established in memory of Rita Kelley, MD (1917-1981), an internationally known cancer specialist who was one of the first women pioneers in medicine at Mass General. She focused on the use of chemotherapy to treat breast cancer and the use of hormones to treat endometrial and other cancers. Noopur Raje, MD, a physician and a leader in clinical research and innovation in the treatment of multiple myeloma, has been named the first incumbent of the chair.

In recognition of the extraordinary 59-year career of Paul C. Zamecnik, MD, at Harvard Medical School and Mass General, an endowed chair in oncology has been established in his name. Dr. Zamecnik was a renowned scientist who discovered tRNA and pioneered the field of antisense technology. He served on the Executive Committee on Research for more than 30 years. Gad Getz, PhD, has been named the inaugural incumbent.

David Ryan, MD, has been named to the Bruce A. Chabner Endowed Chair in Hematology/Oncology. Dedicated to support the chief of the Division of Hematology/Oncology, the chair was established in November 2010 in honor of Bruce A. Chabner, MD, long-time clinical director of the Cancer Center and current director of Clinical Research. As holder of the chair Dr. Ryan succeeds José Baselga, MD, PhD, who in September became physician-in-chief of Memorial Sloan-Kettering Cancer Center.
Initiatives and Events

Rose Murphy, founder of Cure Cancer, is an 11-year pancreatic cancer survivor who was treated at Mass General. In April 2012, she hosted “Let’s Cure Cancer,” a weekend-long event held at The Country Club of Naples and the Stonebridge Country Club in Naples, Florida. Featuring a golf tournament, luncheon, and dinner, the event raised funds to help Cancer Center researchers develop a blood test to detect cancer at an early stage and monitor the response to treatment.

For 15 years, the Mass General Marathon Team, Fighting Kids’ Cancer...One Step at a Time, has raised nearly $8 million to support the Mass General Hospital for Children Cancer Center. Thanks to a strong partnership with John Hancock, the presenting sponsor of the Boston Marathon, 126 runners were able to represent the Cancer Center in the 2012 race. The 2012 team raised more than $760,000 to support pediatric cancer research and patient programs. Leading the team was Dr. Howard Weinstein, chief of Pediatric Hematology/Oncology, who completed his 15th marathon for Mass General and his 22nd marathon overall.

With help from friends like musician Ben Folds and television producer Sam Weisman, Scott Griffith, chairman of the Mass General Cancer Center Leadership Council and former CEO of Zipcar, hosted a high-energy “fun-raiser” in April, the A Cappella Palooza, to raise support and awareness for the Cancer Center. Held at Boston University’s Agganis Arena, the event featured performers from NBC’s music show The-Sing Off.

The Cancer Center celebrated the fifth annual the one hundred gala in June at the Westin Boston Waterfront. Each year, the one hundred honors 100 individuals and groups who have helped advance the fight against cancer. Matt Damon delivered the keynote address for the second straight year. More than 800 people attended this year’s event, raising more than $1.1 million to support cancer research and patient care initiatives. The sixth annual event will be held on June 5, 2013.

In November the Friends of the Mass General Cancer Center hosted the 20th annual Friends Fall Benefit. The featured speakers, Jay and Susan Bolster, discussed the care that Susan and their young daughter, Hope, received while undergoing cancer treatment at Mass General. The Friends is a volunteer organization committed to enhancing the care experience and quality of life of cancer patients and their families. Since its inception the group’s fundraising efforts have topped $5 million, including more than $300,000 raised through this year’s event, East Meets West - Celebrating a World of Care.
In 2012:

» Mass General Cancer Center comprised 24 multidisciplinary disease centers and clinical programs.

» Patients traveled from 67 different countries to receive care at the Mass General Cancer Center.

» Physicians diagnosed and cared for 9,000 new cancer patients.

» Clinicians provided expert, compassionate care during 168,998 outpatient visits and 9,726 inpatient admissions.

» Nurses and patient service coordinators answered 236,348 calls through the Cancer Center Call Center.

» Physician-scientists enrolled 1,040 patients in clinical trials, including 155 patients in phase 1 clinical trials.

» Pathologists conducted SNaPshot screening on 2,000 patients’ tumors to identify “hot spot” mutations on 22 genes that can be targeted with therapy.

» Radiation oncologists delivered 13,372 proton treatments and 57,836 photon treatments to pediatric and adult cancer patients.

» Surgeons performed 10,138 cancer-related surgical procedures.

» Investigators in the Center for Cancer Research published more than 220 peer-reviewed papers, important milestones in advancing understanding of cancer biology.

» Researchers received more than $64 million in funding, including $15 million in competitive grants from the National Institutes of Health/National Cancer Institute (other sources included philanthropy and industry support).

» Donors generously contributed 20,695 gifts totaling $31,136,515.

» the one hundred honored 100 individuals and groups during the 5th annual event to celebrate extraordinary contributions to the cancer community.

» US News & World Report ranked the Mass General Cancer Center among the top 10 cancer providers and named Mass General as the nation’s #1 hospital.
Get Involved!

Nominate! Nominate your cancer hero for the one hundred! To learn more about the event and additional ways to get involved, visit:

» theonehundred.org

Join! The Friends of the Mass General Cancer Center are growing. To learn more about the Friends and ways to get involved, email FriendsofMGHCC@partners.org or call 617.726.1063.

» massgeneral.org/cancer/friends

Run or cheer! The Mass General Marathon Team needs your help to fight kids’ cancer...One Step at a Time. To learn more visit:

» give.massgeneral.org/marathon

Give! Philanthropy plays a vital role in advancing cancer research and patient care at the Mass General Cancer Center. Make a gift today:

» give.massgeneral.org/cancer