Physician-scientists at the Massachusetts General Hospital Cancer Center have been pioneers in the development of new techniques to categorize tumor types by genetic mutation as well as by tissue of origin. This focus on the genetic basis of human cancer has guided drug development and enabled physicians to better predict how individual patients may respond to targeted therapies.

Now Mass General researchers are going beyond gene mutations to delve into the molecular basis of cancer: they are exploring how changes in gene expression linked to the packaging and manipulation of DNA molecules inside the cell nucleus affect disease.

The growing field of epigenetics, which characterizes changes in gene expression caused by mechanisms other than modifications to the underlying DNA sequence, offers the promise of creating even more precise subcategories of cancer. Understanding how epigenetic factors influence the behavior of both normal and cancerous cells is expected to lead to the development of new drugs, especially for patients with recurrent or refractory cancers.

Epigenetics Background

Images of the stained human nucleus in a dividing cell reveal chromosome pairs composed of chromatin, a combination of DNA and vital packaging materials consisting mostly of the proteins known as histones. DNA winds around the histones like thread on a spool, allowing 1.8 meters of DNA to be packaged in the confines of each cell nucleus.

Historically, scientists believed that the packaging materials bundling DNA were relatively inert, but studies have shown that these dynamic materials play a central role in determining cell fate during development, and in altering gene expression over the lifetime of a cell. Epigenetics is revealing how chromatin proteins help ensure that each cell type expresses only those genes that it needs to carry out its own special functions, and how chromatin failures—switching genes on or off at the wrong time—may result in birth defects or cancer.

continued on the next page
Gene-Expression and DNA Methylation in Glioblastoma Cancer Stem Cells

Developing clinical solutions based on understanding of the processes reshaping chromatin over the lifetime of a cell. Bradley E. Bernstein, MD, PhD, a pathologist at Mass General and Early Career Scientist of Howard Hughes Medical Institute, explores chromatin organization at a global level.

In 2007, Dr. Bernstein, who is also an affiliate of the Broad Institute in Cambridge, was part of the first group of scientists to use ultrahigh throughput sequencing to map epigenetic patterns across the entire genome of mouse and human cells. This effort led to a large-scale project sponsored by the National Institutes of Health to characterize the epigenomes of many cell types. Using conventional ultrahigh throughput methods for this purpose, however, damaged the cells’ DNA, so that millions of cells were required to ensure a sufficient sample size for analysis.

Chromatin Profiles in Wilms Tumor

In 2010, Dr. Bernstein and his colleagues from the Mass General Cancer Center, the Broad Institute and Harvard Medical School published one of the first studies examining the chromatin landscape of a tumor. The group selected Wilms tumor, a form of pediatric kidney cancer. The study revealed that, from an epigenomic perspective, Wilms tumor cells bear a striking resemblance to a normal kidney stem cell. The researchers suspect that many pediatric tumors arise when epigenetic programming during development goes awry.

Chromatin Changes Resulting from RB Loss Cause Defects in Chromosome Segregation

Nicholas J. Dyson, PhD, a geneticist in the Mass General Center for Cancer Research, and his colleagues study the retinoblastoma (RB) family of proteins. RB was one of the first tumor suppressor genes identified; loss of the product of this gene, pRB, results in tumor formation and has been linked to genomic instability.

Inherited RB mutations create an increased risk for childhood retinoblastoma (the disease for which the gene was named), osteosarcoma, melanoma and brain tumors. Sporadic RB mutations have been found in small-cell and non-small-cell lung cancer, as well as breast, prostate and bladder cancers. Other forms of cancer have been found to have defects in the regulation of pRB even if the gene itself is not mutated. Further analysis of how pRB affects genome stability may reveal new therapeutic targets for a broad range of tumor types.

In one recent study, Dr. Dyson and his colleagues Amity L. Manning, PhD, and Michelle S. Longworth, PhD, used human cell lines to probe for a link between pRB loss and tumor progression. Their research revealed that inactivation of the RB gene affects mitotic cell division, a point in the cell cycle that is not typically associated with pRB activity.

In normal mitosis, the compact chromatin structure enables paired sister chromatids (the identical daughter strands of a replicated chromosome) to attach to the mitotic machinery as the cell prepares to separate into two daughter cells.

In pRB-deficient cells, the centromere, which contains the chromatin holding the sister chromatids together, is less rigid, promoting improper attachment of chromatids to the mitotic machinery and leading to chromosome segregation errors. As a result, one daughter cell may have too many chromosomes and the other too few (both conditions known as aneuploidy). A hallmark of many cancer cells, aneuploidy is associated with metastasis, poor patient response to chemotherapy and poor prognosis.

The Dyson lab is exploring whether certain drugs might suppress the effects of the RB mutation—to stabilize the genome during cell division—or cause the abnormal cells to undergo apoptosis, or cell death. Further understanding of RB’s regulation of...
mitotic fidelity could reveal important new directions for cancer drug development.

Using Histone Modifications for Diagnosis and Treatment

Johnathan R. Whetstine, PhD, a geneticist at the Mass General Center for Cancer Research, studies the relationship between enzymes that regulate the chemical modification of histones and cancer. Different combinations of histone modifications alter chromatin structure, facilitating gene transcription or silencing of genes.

Dr. Whetstine is primarily interested in enzymes that regulate genes by adding or subtracting methyl groups. The activity of these enzymes, known as methyltransferases and demethylases, respectively, are tightly controlled by the cell.

Aberrant methylation is associated with a variety of human diseases, including cancer. Compounds that hypomethylate DNA, such as decitabine, are used effectively in clinical settings to treat hematopoietic diseases, including myelodysplastic syndrome and acute myelogenous leukemia (AML). As yet, no agents targeting histone methyltransferases or demethylases have progressed into clinical trials.

Dr. Whetstine and colleagues focus on a family of histone demethylases known as the KDM4/JMJD2 family, which are amplified in human cancers.

Recent studies by the lab have revealed new functions for the KDM4/JMJD2 enzymes. Previous research had suggested that the enzymes acted primarily in gene regulation; however, the group's new studies have shown that members of the family significantly impact chromatin structure and cell cycle regulation, including the timing of DNA replication. The Whetstine lab first explored these activities in the worm model C. elegans, and then demonstrated that they also occur in cultured human cells.

The discovery of unexpected roles for these enzymes in cell culture opens new avenues for deciphering how they behave in human diseases. Dr. Whetstine emphasizes that individual methyltransferases and demethylases act in very specific ways. Deepening our understanding of their role in cancer should enable scientists to develop targeted drugs that have fewer side effects than drugs that target enzymes with broad functions throughout the cell.

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Adjuvant Radiation Enhances Surgical Management to Reduce Recurrence of Primary Chordoma

Chordoma is a slow-growing bone tumor that may occur anywhere along the spine. Believed to arise from the cellular remnants of the embryonic notochord, chordoma is a very rare cancer, with only 300 new cases diagnosed in the United States each year. While surgery has traditionally been the primary mode of treatment, Massachusetts General Hospital has helped pioneer the combination of radiation therapy with surgical treatment. Oncologists have so far seen limited treatment benefit with traditional chemotherapy.

In 2009, the Massachusetts General Hospital Cancer Center opened one of the country’s first multidisciplinary centers dedicated to managing patients with this difficult-to-treat cancer. The Stephan L. Harris Center for Chordoma Care, part of the Center for Sarcoma and Connective Tissue Oncology, brings together orthopaedic oncologists, neurosurgeons, general and reconstructive surgeons, medical oncologists, radiation oncologists, musculoskeletal radiologists and surgical pathologists, nurse practitioners and other health professionals experienced with chordoma.

Adjuvant Radiation Improves Surgical Outcomes

Francis J. Hornicek, MD, PhD, is director of the Harris Center and co-director of the Center for Sarcoma and Connective Tissue Oncology, where each patient receives individualized treatment provided by a multispecialty team. Treatment for mobile spine and sacral chordomas routinely involves surgery and a combination of proton and photon radiation therapy before and after surgery. This protocol is for patients who have not previously had surgical treatment.

Preoperative radiation appears to “sterilize” the operative bed so that any malignant cells left behind in the resection site are unable to grow again. Postoperative radiation destroys any remaining tumor cells to help reduce the rate of recurrence.

Patients receive preoperative radiation for two to five weeks. Careful coordination of surgery and radiation treatment protocols is crucial, since preoperative radiotherapy can increase the risk of wound-healing complications after resection. Surgery can take place immediately after a two-week course of neoadjuvant radiation. A five-week course requires a three- to four-week delay to allow the skin and surrounding soft tissues to recover.

Patients undergo surgery with the goal of complete tumor resection, preferably through an en bloc procedure (removal in one piece), the standard treatment for chordomas of the spine. Given their expertise and precision, Harris Center surgeons achieve low rates of involved surgical margins with less morbidity and blood loss.

Even with meticulous resection techniques, however, tumor size and location may make it impossible to attain a noncontaminated margin. The surgical goal then becomes gross tumor resection.

For example, some skull-based chordomas are extremely difficult to remove in one piece. With sacral chordomas, the tumor may involve nerves controlling the bowel or bladder. These cases may require removal of the nerves, along with the tumor, resulting in the need for an ostomy in some patients, or other measures. Approximately four weeks after surgery, patients receiving the combined treatment protocol move on to two to five additional weeks of proton beam therapy.

For patients with high sacral tumors and intact neurological function, an investigational approach using higher dose photon/proton radiation without surgery is available. This approach has controlled a high proportion of the tumors with preservation of bowel and bladder function and avoidance of an ostomy. However, additional follow-up on these patients is needed to fully determine how durable this investigational treatment proves to be and to assess long-term neurologic function, which may be affected by the high-dose radiotherapy.

Historically, chordoma patients who had surgery alone experienced a high rate of recurrence. Outcomes at the Harris Center have shown significant improvement with the addition of neoadjuvant and adjuvant radiation. Among Harris Center patients enrolled in the combined protocol who have not had any previous surgical treatment, there have been no local recurrences to date.
Advances in Intraoperative Radiation

In the 1970s, Herman D. Suit, MD, PhD, former chief of Radiation Oncology at Mass General, helped revolutionize chordoma treatment by pioneering the use of radiation as adjuvant therapy. Today, Thomas F. DeLaney, MD, co-director of the Center for Sarcoma and Connective Tissue Oncology, and colleagues including Yen-Lin E. Chen, MD, and Norbert J. Liebsch, MD, PhD, are leading the development of new radiation therapies targeting chordomas.

Dr. DeLaney and his team have devised several innovative methods to plan and deliver effective doses of radiation while preserving the integrity and function of adjacent nerves, as well as bony and visceral structures intimately associated with many chordomas.

One such critical advance is the use of intraoperative radiation of the dura, which covers the spinal cord. This technique is particularly indicated for chordomas arising from the cervical, thoracic and upper lumbar spine. Typically, when physicians use external beam radiation on these tumors, they are limited in the radiation dose they can deliver because the spinal cord is sensitive to radiation. However, Mass General radiation oncologists developed a brachytherapy device called a dural plaque that allows them to safely give higher doses of radiation during surgery after the tumor has been removed. The custom-designed device, which uses phosphorus-32, is applied to the dura for 10 minutes. The technique has been well-tolerated by patients and adopted by other hospitals.

Intensity-Modulated Proton Therapy to Treat Chordoma

Another new treatment under way is intensity-modulated proton therapy (IMPT). Beginning in 2011, the Francis H. Burr Proton Therapy Center at Mass General will be one of the first proton centers in the United States to offer IMPT for spine and skull-based sarcoma patients, including those with chordomas. IMPT may benefit chordoma patients by allowing radiation oncologists to better shape and modulate the proton beam to spare the spinal cord and nerves while delivering high doses of radiation to the tumor bed.

Dr. DeLaney is also leading a pilot study at the Harris Center to determine if dosimetry planning for patients with chordomas or other types of sarcomas can be improved using IMPT, compared with plans using three-dimensional, passively scattered protons. This study involves reviewing archived radiation treatment CT scans and then using computer simulations of the different techniques for dose delivery with protons.

In addition, Dr. DeLaney and colleagues are enrolling patients in a study to determine the feasibility of using specialized PET imaging to identify regions of hypoxia, or low oxygen levels, within a chordoma tumor. They will then analyze whether a dose-painting/IMPT approach could effectively deliver an escalated radiation “boost” dose to hypoxic regions—which are typically radiation-resistant—while sparing normal tissue. Those treatment scenarios will be compared with IMPT based on CT and MRI imaging alone.

Searching for Effective Chemotherapy and Genetic Clues

Another challenge in the management of chordoma is that there are no effective chemotherapy options available. Unlike other types of sarcoma, no specific tumor-suppressor gene or oncogene has so far been linked to chordoma.

However, translational research by Harris Center investigators is yielding a better understanding of the molecular biology of chordoma. One asset in this effort is the chordoma tissue bank established by the Massachusetts General Hospital.

Key Points

- The Stephan L. Harris Center for Chordoma Care is one of the country’s first multidisciplinary centers dedicated to the diagnosis and treatment of this rare cancer.
- Physician-researchers at the Harris Center pioneered the use of adjuvant radiation with surgery for chordoma, which is associated with zero recurrences to date among patients who have received initial chordoma treatment at the center.
- Mass General radiation oncologists were the first to develop a technique for effective intraoperative radiation of the dura.
- Beginning this year, the Francis H. Burr Proton Therapy Center at Mass General will be one of the first proton centers in the country to offer intensity-modulated proton therapy for chordoma patients.
- The Harris Center also serves as a hub for clinical trials and translational research based on new understanding of pathways that contribute to tumor growth, such as the mTOR and PDGFR pathways.
Adjuvant Radiation Enhances Surgical Management to Reduce Recurrence of Primary Chordoma

sarcoma group. One of the largest known such archives, it includes tissues from more than 100 chordoma cases.

Edwin Choy, MD, PhD, director of sarcoma research, and his colleagues are studying the genetics of chordoma, including the abnormalities that define the behavior of chordoma cells. Dr. Choy’s team uses high-throughput genomic sequencing technology to look at the genetic alterations in chordoma tissue, an effort that is generating a catalog of tumor drivers and suppressors. The findings could lead to potential targets for new chordoma therapies.

Some of the current research focuses on understanding pathways contributing to tumor growth, such as the molecular pathway known as mTOR (mammalian target of rapamycin). Researchers have shown that this pathway plays a key role in controlling growth and metabolism in normal cells, and that it behaves abnormally in many cancers. Joseph Schwab, MD, and Vijaya Ramesh, PhD, are among the researchers at the Mass General Cancer Center who are exploring mTOR’s potential role in chordomas.

Another target of interest is the platelet-derived growth factor receptor, or PDGFR. Harris Center physicians are engaged in clinical studies of PDGFR pathway inhibitors. For example, Dr. Choy’s team recently completed a multicenter, phase 2 trial of the PDGFR inhibitor dasatinib in patients with chordomas and other advanced sarcomas. Future trials will likely focus on other promising PDGFR-targeting agents combined with radiation.

Compassionate Support for Patients

While access to advanced treatments is critical, chordoma patients often need other types of support to cope with this frustrating, and sometimes isolating disease. The community of health professionals and fellow patients at the Harris Center offers a wealth of information, counseling and understanding for chordoma patients and their families.

Contributors


Addressing Challenges, Improving Quality of Life for Breast Cancer Patients

Novel approaches developed by physicians at the Mass General Cancer Center are improving quality of life for breast cancer survivors. In addition to providing patients with state-of-the-art therapies, Mass General oncologists, radiation oncologists and surgeons are collaborating to minimize the long-term challenges that often accompany lifesaving breast cancer therapies, including lymphedema (chronic swelling of the arm due to blocked lymph vessels), concerns over chest or breast disfigurement, and chronic pain.

Breast cancer is the most common cancer among women in the United States after nonmelanoma skin cancers. It affects approximately one in every eight women over the course of a lifetime. Despite its prevalence, however, the incidence of breast cancer has declined since 1998. In addition, dramatic advances—genetic identification, early and accurate diagnoses and effective therapies—have increased the estimated relative 10-year survival rate of women diagnosed with early breast cancer to nearly 90 percent.

Statistics regarding breast cancer survival are encouraging, but they do not address the impact of the disease on the woman as a whole. Eliminating cancer is often not the end of a woman’s struggles with the disease. Many breast cancer survivors face significant physical and emotional challenges long after treatment.

Mass General Cancer Center physicians and researchers are working together to help reduce posttreatment problems with new approaches to lymphedema prevention and management, nipple-sparing mastectomy and pain management.

Advances in Prevention and Management of Lymphedema

Lymphedema is swelling that can occur in the arm, breast or trunk of the body on the side that has been treated for cancer. It is thought to occur when lymph vessels become compromised and can no longer transport the daily load of lymph fluid. It is a potentially irreversible complication of breast cancer treatment. Studies confirm that lymphedema can hinder arm function, and have a devastating psychological effect on patients, serving as a lifelong reminder of the cancer.

The rate of lymphedema has declined in recent years due to the relative increase in breast-conserving surgeries compared with modified radical mastectomies. Also, extensive lymph node dissection, a major cause of lymphedema, generally has been replaced with sentinel node biopsy. Still, lymphedema persists and may have dramatic impact on quality of life.

Traditionally, the problem has been considered a complication for physical and occupational therapists to manage, but physicians and other medical staff at the Mass General Cancer Center have taken a more comprehensive approach. In 2009, this commitment resulted in a $2.2 million National Institutes of Health grant to support the work of the lymphedema prevention and treatment team at Mass General.

The Importance of Early Lymphedema Screening

Led by Alphonse G. Taghian, MD, PhD, chief of Breast Service for the Mass General Department of Radiation Oncology, the Lymphedema Studies team has developed one of the first lymphedema screening programs in the country. Typically, lymphedema is diagnosed only when it is visually apparent, at which point treatment is often ineffective. The focus of the Cancer Center’s screening program is to diagnose the condition in its subclinical state when early intervention can prevent development of clinical signs and symptoms.

Improving Treatment Planning

In their study of breast cancer-related lymphedema, Mass General Cancer Center researchers have determined that undergoing lymph node dissection or radiation to the lymph nodes increases a woman’s risk of developing lymphedema. Up to 8 percent of patients who have sentinel node biopsies and 20 to 25 percent of women with axillary lymph node dissection develop lymphedema at some time after treatment. Adjuvant radiation therapy and postoperative infection increase the risk of developing lymphedema.

Before cancer surgery, Mass General clinicians take a baseline measurement of a woman’s arm. This baseline measurement and periodic measurements after treatment are vital to accurate diagnosis. The measurement takes just three minutes using a perometer—a device that employs infrared technology to accurately verify arm volume.

Since the program began in 2005, Mass General Cancer Center experts have screened more than 2,200 breast cancer patients for lymphedema. Arm measurement, which is now part of the Cancer Center’s standard clinical evaluation, has helped Dr. Taghian’s team better identify and treat the condition and also has led to greater understanding of the risk factors involved.

A potentially irreversible form of disfiguration, lymphedema can hinder arm function and is often diagnosed too late for treatment to be effective. The women pictured above experienced arm volume increases of 31 percent (left) and 54 percent (right).
lymphedema, as does having a body mass index of more than 25.

Currently, women who have unilateral, nonmetastatic breast cancer are being invited to participate in a phase 3 clinical trial focused on establishing evidence-based treatment plans for lymphedema. One goal is to determine whether early intervention, such as wearing a compression sleeve for 12 weeks, can prevent progression of the condition.

Women who progress to moderate lymphedema may be asked to participate in a second phase of the study, which seeks to determine whether more aggressive measures, such as nightly bandaging, massage and compression—in addition to wearing a sleeve—are beneficial.

Identifying a New Form of Lymphedema

During the course of their work, Dr. Taghian and his team have noticed that some women experience a transient form of the condition; they show signs of subclinical lymphedema but do not progress to clinical symptoms. The Mass General researchers have studied the characteristics of patients who have transient lymphedema and those whose lymphedema becomes permanent. Distinguishing the two groups is critical to ensuring that women do not receive unnecessary treatment. Study results, currently submitted for publication, should assist physicians in identifying those patients whose lymphedema is not expected to progress.

Innovations in Nipple-Sparing Mastectomy

Nipple-sparing mastectomy (NSM), in which breast tissue under the skin is removed while leaving the nipple in place, yields a more natural-looking reconstructed breast. It has not been widely performed in the United States in recent years due to early concerns that it might increase the risk for cancer recurrence. As a result, removing the nipple during a mastectomy had become routine.

More recently, however, there has been renewed interest in the NSM approach, particularly among women who have chosen prophylactic surgery in response to genetic testing or who have opted for mastectomy over lumpectomy. Nipple-sparing surgery, coupled with a saline or silicon implant, provides a more natural-looking breast, bolstering self-esteem and patient satisfaction. The key challenge with the procedure is to achieve the oncologic goal of eliminating the tumor and minimizing recurrence while preserving the integrity and blood supply to the nipple.

Mass General Cancer Center physicians believe nipple-sparing mastectomy is an important option for breast cancer patients. They have conducted extensive research to advance both the safety and efficacy of this technique.

Identifying Nipple Anatomy

Previous efforts to preserve a healthy nipple while removing as much duct tissue as possible to prevent cancer recurrence were complicated by lack of knowledge about nipple anatomy. That changed with an extensive study led by Barbara L. Smith, MD, PhD, director of the Mass General Cancer Center’s Breast Program. Published in 2009 in the Journal of Clinical Oncology, the study provided critical information for surgeons undertaking this approach.

Through a meticulous anatomical analysis of more than 300 postmastectomy nipples, Mass General researchers created a series of three-dimensional nipple reconstructions identifying ducts and blood vessels required for preservation of the nipple. In addition to providing essential new anatomical detail about nipples, this analysis assessed the clinical and pathologic factors associated with cancer in the nipple for patients undergoing mastectomy. Mass General researchers concluded that cancer in the nipple is likely to occur in association with HER-2 receptor amplification, smaller tumor distance from the nipple and larger size of the lesion.

Changing the Way Nipple-Sparing Surgery Is Performed

After concluding their anatomical research, Mass General Cancer Center researchers began to test the efficacy of various surgical techniques on resected nipple specimens. They explored new methods to best remove ducts connecting with the nipple while preserving the nipple’s blood supply. The surgical guidelines they developed are now used by other breast surgeons who perform nipple-sparing mastectomies.

Improving Prediction of Cancer Risk

Based on their 2009 analysis of clinical and pathologic risk factors, the Mass General researchers also developed a risk assessment tool. The tool—or “calculator”—helps surgeons assess the risk for nipple involvement by tumor so that they can determine whether nipple-sparing surgery is advisable.

Physicians at the Mass General Cancer Center are now drawing on their extensive surgical experience to establish a nipple-sparing mastectomy registry. The registry will track long-term outcomes and patient satisfaction with nipple-sparing surgery.

Improving Pain Control

Mass General Cancer Center physicians have made advances in effective pain control for breast cancer patients undergoing mastectomy with immediate reconstruction. One option offered to these patients is the paravertebral block (PVB).

PVB is an advanced nerve block technique, in which long-acting local anesthetic is injected below the muscles lateral to the spine and adjacent to the spinal nerves. Ultrasound guidance ensures correct needle placement, and the injected local anesthetic provides a band of numbness around the chest and breast area. The block is not a new technique, but has risen in popularity in the past 10 years due to advances in ultrasound technology that have increased both its accuracy and

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Key Points

- The Mass General Cancer Center is addressing the ongoing physical and psychological challenges that can impact quality of life for breast cancer patients.
- Led by Alphonse G. Taghian, MD, PhD, the Mass General Cancer Center developed one of the country’s first programs for lymphedema screening, prevention and treatment.
- Under the leadership of Barbara L. Smith, MD, PhD, the Cancer Center has developed surgical guidelines providing safe and effective techniques for nipple-sparing mastectomies.
- The Mass General Cancer Center has developed a dedicated team to administer paravertebral block to breast surgery patients to reduce postoperative pain and speed recovery.
safety. It is administered prior to general anesthesia for supplemental pain control.

Research on Patient Benefits
The Cancer Center has found that in addition to offering effective, acute postoperative pain control, the paravertebral block offers additional benefits. It decreases the need for narcotics to control pain, so patients have less nausea and vomiting than with general anesthesia alone. PVB may also reduce the risk for chronic pain, facilitating earlier mobilization and faster hospital discharge. Michelle C. Specht, MD, surgical oncologist, and Katharine H. Fleischmann, MD, anesthesiologist, are preparing a formal study to examine this hypothesis.

A Dedicated Block Service Team
Some hospitals choose not to offer the paravertebral block because setting up the procedure can delay surgery. At Mass General, Lisa Warren, MD, director of Ambulatory and Regional Anesthesia, and her team have developed a dedicated block service that includes anesthesiologists and nurses. The team follows a systematic approach to ensure safety and improve efficacy of the block. As a result, the Mass General Cancer Center is able to offer the paravertebral block to 100 percent of patients undergoing mastectomy with immediate reconstruction.

The advances made in each of these areas—lymphedema prevention, nipple-sparing mastectomy and increased access to the paravertebral block—can significantly impact the quality of life of breast cancer patients. Such innovations are critical as Mass General Cancer Center physicians strive to address the full range of challenges that may arise for patients after breast cancer therapy. •

Selected References


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Cord Blood Transplantation: A Viable Approach for Hematologic Cancers

For patients with leukemia, lymphoma or other hematologic cancers, an allogeneic hematopoietic stem cell transplant—receiving blood stem cells from another individual—may be the only curative treatment option available. There are three transplant sources for these patients: adult bone marrow stem cells, adult peripheral blood stem cells and umbilical cord blood stem cells.

Although the potential benefits of stem cell transplantation are significant, finding an appropriately HLA-matched (human leukocyte antigen) stem cell donor is often difficult. Only 30 percent of those needing a stem cell transplant have a matched unrelated donor in their family, and only 50 percent of those needing a stem cell transplant have a matched related donor. Finding a matched unrelated donor is often difficult. Only 30 percent of those needing a stem cell transplant have a matched donor in their family, and only 50 percent of those needing a matched unrelated donor (i.e., within the National Marrow Donor Program, marrow.org). Among minority patients, the likelihood of finding a matched unrelated donor can be even more limited—just 10 to 20 percent—because of a lack of minority representation within the bone marrow registry.

For those patients unable to find a matched related or unrelated donor, an alternative transplant source is required. The umbilical cord is a rich source of hematopoietic stem cells and provides the opportunity for umbilical cord blood transplantation (CBT).

The first cord blood transplant was performed on a child with Fanconi’s anemia in France in 1988. Since then, the use of this approach has expanded exponentially, and CBT is now an accepted therapy for both adults and children. More than 25,000 cord blood transplants have been performed to date worldwide, and Boston has become a leading center for CBT treatment. Approximately 40 percent of CBT recipients are cured of their underlying cancers.

Setting the Standard for CBT

Karen K. Ballen, MD, clinical director of the Leukemia Center at the Mass General Cancer Center, is an international leader in cord blood transplantation and launched Mass General’s cord blood transplantation program.

Dr. Ballen participated in the development of the national CBT standards. She continues to work with the National Marrow Donor Program, marrow.org). Among minority patients, the likelihood of finding a matched unrelated donor can be even more limited—just 10 to 20 percent—because of a lack of minority representation within the bone marrow registry.

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Dr. Ballen participated in the development of the national CBT standards. She continues to work with the National Academy of Sciences, the American Society of Blood Banks and the American Society of Bone Marrow Transplantation on CBT regulations and treatment guidelines.

For eight years, Dr. Ballen and her colleagues at the Mass General Cancer Center have collaborated with other Boston institutions through the Dana-Farber/ Harvard Cancer Center consortium to conduct research aimed at improving CBT methods. They work jointly on clinical trials, research protocols and standards of care.

At Mass General, advanced clinical and research studies are enhancing the benefits of CBT and overcoming challenges with measures such as double cord blood transplantation (DCBT), new pretransplant conditioning protocols for transplant recipients, and better methods of monitoring and eliminating infection.

Cord Blood Transplantation Benefits

CBT is an effective alternative stem cell source for several reasons. A safe, effective CBT can be performed with a partially matched cord blood unit, compared with the nearly 100 percent match adult stem cells require. This difference results from the immaturity of cord blood immune cells, which are less likely than mature immune cells to immediately attack the transplant recipient’s vital tissues, causing the condition known as graft-versus-host disease, or GVHD. The ability to move forward with a less closely matched patient and donor improves the chance of finding an acceptable transplant stem cell source.

Cord blood is also more readily available than other stem cell sources, so that a transplant can be scheduled according to the patient’s clinical needs rather than the donor’s availability. When parents choose to donate their newborn child’s cord blood, the sample is sent to a public bank and frozen for later use. The cord blood can be shipped to any hospital throughout the world for transplant use within a few days. Other stem cells sources, such as adult bone marrow or peripheral blood stem cells, can take six to eight weeks or longer to arrive.

Though a bone marrow match or stem cell match can be identified quickly through the registry database, the rest of the process may be cumbersome. The donor must be located, must have a blood test confirming the match and undergo a physical exam, and must participate in a discussion of the risks, albeit minor, of bone marrow or peripheral blood stem cells donation. Then the extraction or collection procedure must be scheduled. The potential stem cell transplant may be delayed or prevented at any point.

In addition to its availability, cord blood offers several clinical benefits. The reduced tendency to cause chronic GVHD because cord blood stem cells are more immunologically naïve may affect the quality of life and long-term survival of stem cell transplant recipients. Preliminary research also suggests that the cancer relapse rate among CBT patients may be
lower than with transplant from either bone marrow or blood stem cells. This is particularly significant because the relapse rate after other types of transplant has tended to be inversely proportional to the development of chronic GVHD.

Important clinical outcomes are also encouraging. Preliminary work led by medical oncologist Yi-Bin A. Chen, MD, of the Mass General Cancer Center’s Bone Marrow Transplant Program, in collaboration with the Dana-Farber/Brigham and Women’s Cancer Center, has indicated overall survival and disease-free survival rates for CBT are similar to those for other types of transplantation. The preliminary review of patient data over a six-year period compared results of CBT, matched related donor, and matched unrelated donor transplants for patients receiving a reduced-intensity conditioning regimen.

**CBT Risks and the Promise of DCBT**

Although there are potential long-term advantages to CBT, the risk of infection can be high. The number of hematopoietic stem cells can be collected from a single umbilical cord is far less than can be collected from an adult donor. Furthermore, while the immaturity of the cells decreases the risk of chronic GVHD, the transplanted cord blood cells take longer to mature and divide than cells from adult donors, leading to an extended recovery time and an increased possibility of infection in the transplant recipient.

Given the low stem cell number derived from each umbilical cord, all adult recipients enrolled in the joint protocols receive stem cells from two cords in a process termed double cord blood transplantation (DCBT). The two unrelated cord blood units are both partially matched with the recipient and partially matched with each other. DCBT increases the donor stem cell count and speeds engraftment, the recovery of normal blood cell production in the recipient. Faster engraftment decreases the risk of infection in the recipient and may decrease the risk of disease relapse, though this has not been proven definitively.

Expanding the concentration of stem cells in cord blood units is a research priority nationally. A team from the Mass General Cancer Center, Dana-Farber/Brigham and Women’s Cancer Center and Dana-Farber/Children’s Hospital is exploring a means of expanding the number of stem cells from an individual cord. Their research is aimed at determining whether this expansion of the stem cell count can help to speed recovery of the immune system following transplantation.

**Targeting Infections**

In addition to enhancing stem cell count, Mass General Cancer Center researchers are working to better manage infections among CBT patients. The use of new antibiotics and antifungal agents to prevent infections has helped move more patients past the initial, most vulnerable stage of CBT recovery. Close posttransplant monitoring also helps to quickly identify and treat potential infections that might arise.

Together, these improvements in the transplant standards of care have reduced transplant-related mortality in the first 100 days posttransplant from 40 percent 10 years ago to 13 percent today.

To further reduce the risk of infection and other transplant-related complications, Thomas R. Spitzer, MD, director of the Mass General Cancer Center Bone Marrow Transplant Program, has helped pioneer reduced-intensity conditioning regimens for stem cell transplantation.

Historically, conditioning patients for a stem cell transplant has involved an aggressive program of chemotherapy and radiation. Researchers believed that this intensive therapy would destroy the residual cancer and make room for the new immune system.

The therapy had many side effects, however, and made it difficult for patients, continued on page 16
Cancer Center Study Reveals New Drug Resistance Mechanisms in EGFR-Positive NSCLC

New types of drug resistance mechanisms have been identified by Massachusetts General Hospital Cancer Center researchers, who reported on their study of drug resistance in patients with non-small-cell lung cancer (NSCLC) in Science Translational Medicine in March. Their investigation of lung tumors that had become resistant to targeted therapies revealed unexpected genetic and phenotypic changes in response to treatment. They also discovered that resistance-conferring genetic mutations can disappear when treatment is discontinued.

The research team led by thoracic oncologists Lecia V. Sequist, MD, MPH, and Jeffrey A. Engelman, MD, PhD, monitored the molecular status of the tumors with repeat biopsies after cancers became resistant to therapies. Their findings suggest that such serial biopsies—performed throughout the course of a patient’s disease—may be an essential tool in the search for how to reverse or prevent drug resistance. Their investigation focused on patients whose cancers had an EGFR mutation, who represent 12 percent of NSCLC patients.

The targeted therapies erlotinib (Tarceva) and gefitinib (Iressa), both tyrosine kinase inhibitors (TKIs), have significantly halted tumor growth for most EGFR-positive patients, but drug resistance typically emerges within a year and tumor growth resumes. Two mechanisms for this resistance were previously identified: a second EGFR mutation blocking TKI activity and overproduction of the MET oncogene. There also have been clinical reports of resistant tumors “regaining” sensitivity to EGFR TKIs after a prolonged respite from the medicine.

To examine the molecular basis of drug resistance, the researchers compiled genetic and phenotypic tumor profiles for the 37 study patients, analyzing biopsy samples prior to TKI treatment and after resistance emerged. While confirming the presence of the previously identified mutations, the results revealed two novel genetic changes—mutations in the PIK3CA oncogene and overproduction of the EGFR molecule itself.

Striking histologic changes were also documented. In five samples, the NSCLC cells had been converted into small-cell lung cancer (SCLC) cells, which are more responsive to different chemotherapies. In two patients, the tumor cells appeared to undergo a morphological change, transforming them from epithelial into mesenchymal cells. This kind of transformation has been linked to metastasis, but is not commonly thought to be linked to drug resistance.

The study suggests serial biopsies may be a valuable tool to interrogate the changing nature of drug response and resistance in oncogene-driven cancers, noted Dr. Sequist. Repeating biopsies throughout treatment may contribute to a greater understanding of acquired resistance and also may help physicians decide “whether resumption of targeted therapy or initiation of a standard therapy would be most appropriate for an individual patient,” she added.

A human breast cancer cell undergoing asymmetric division to produce a “sleeping” daughter cell (dark blue center). Cancer Center researcher Sridhar Ramaswamy, MD, seeks to identify the genetic and signaling networks that trigger dormancy, rendering cancer cells treatment resistant.

Sridhar Ramaswamy, MD, Awarded Stand Up to Cancer Grant to Study ‘Sleeping Cancer Cells’

For his investigation of cancer cells that are dormant, or “sleeping,” Mass General Cancer Center researcher Sridhar Ramaswamy, MD, has been awarded a Stand Up to Cancer (SU2C) Innovative Research Grant. This year’s SU2C high-risk/high-reward translational research grants were announced at the American Association for Cancer Research (AACR) annual meeting in April.

Dr. Ramaswamy’s work focuses on the switch between sleep and wakefulness in virtually all cancer cell types. When in a dormant state, cancer cells are treatment-resistant. The Ramaswamy lab is working to identify the genetic and protein signaling networks that trigger and maintain cell dormancy. Learning how to prevent cancer cells from becoming dormant, so that they remain susceptible to drug therapy—or how to kill them while they sleep—could yield new diagnostic or drug therapy approaches.

EGFR-mutant non-small-cell lung cancer cells (left, prior to TKI therapy) have become TKI resistant after treatment (right) and display a phenotype change to SCLC, which is responsive to some chemotherapies.


Editorial Support for ADVANCES at the MASS GENERAL CANCER CENTER

The following Cancer Center clinicians and researchers contributed editorial support to the publication of ADVANCES at the MASS GENERAL CANCER CENTER in 2010 and 2011: Oncology Fellow Ryan B. Corcoran, MD, PhD; Oncology Fellow Andrew A. Lane, MD, PhD; Surgical Oncology Fellow Nicole Look Hong, MD; Radiation Oncology Resident Jona A. Hattangadi, MD; Radiation Oncology Resident Nils D. Arvold, MD; Hematology Fellow David B. Sykes, MD, PhD; and Postdoctoral Research Fellow Amy L. Manning, PhD.
Mass General Cancer Center Collaboration with Veridex and Johnson & Johnson Will Build on Circulating Tumor Cell Technology

Massachusetts General Hospital has launched a collaboration with Veridex, LLC, a Johnson & Johnson company, to develop new Circulating Tumor Cell (CTC) technologies. Found at extremely low levels in the bloodstream, CTCs are solid tumor cells that may offer a key to early detection and noninvasive characterization of cancer.

At Mass General, the collaboration is led by the BioMicroElectroMechanical Systems (BioMEMS) Resource Center and the Cancer Center. Veridex will provide expertise with clinical validation and regulatory clearance to a newly created Center for Excellence in CTC Technologies. The Mass General team is highly experienced in CTC studies, having developed microfluidic technologies supported by a multi-institutional grant from Stand Up to Cancer, a national fundraising effort sponsored by the Entertainment Industry Foundation.

“Applying data gathered from CTCs to the care of cancer patients is a complex challenge,” said Mehmet Toner, PhD, director of the Mass General BioMEMS Resource Center. “Our multidisciplinary team is in a unique position to take this on.”

Bruce A. Chabner, MD, Declares ‘Rare Tumor’ Concept Is Transforming Cancer Drug Development

Mass General Cancer Center Director of Clinical Research Bruce A. Chabner, MD, received the Herbert and Maxine Block Memorial Lectureship Award in March. Given each year to a distinguished cancer researcher, the prize honors the Block Family, a major benefactor of the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute. In his Block Lecture, Dr. Chabner said drug development is being rapidly transformed by our evolving understanding of how cancer develops at a molecular level.

“We now know that the traditional classification of tumors based on tissue of origin confers limited information, and that each histological cancer type encompasses a diverse group of uncommon or rare tumor types driven by a specific genetic mutation, amplification or translocation,” he said. “These genetic changes ‘drive’ tumor growth and dissemination.”

“But we now have drugs that specifically block these drivers,” Dr. Chabner added. “Our recent lung cancer and melanoma trials illustrate that early trials can be remarkably successful—and prove the value of new drugs—if we are able to select patients whose tumors have the targeted genetic changes. Our thinking has shifted away from seeking one drug to treat many types of cancer. Successful drugs for the future will likely target these relatively rare tumors harboring specific mutations.”

Discovery of RNA ‘Satellite Repeats’ Could Yield Universal Cancer Tumor Marker

Massachusetts General Hospital Cancer Center researchers have discovered a previously unknown feature of common tumor cells—massive overexpression of certain DNA sequences. Called “satellite repeats,” these sequences were not previously suspected of having a role in cancer. While active in DNA transcription—or conversion—into RNA, satellite repeats are inactive in normal adult cells.

In the journal Science last January, however, a research team led by Daniel A. Haber, MD, PhD, director of the Mass General Cancer Center, reported that satellite repeats are active and massively overexpressed in cancer cells. Such overexpression characterized multiple tumor types, suggesting that it could eventually be used as a biomarker for early diagnosis and analysis of tumor development.

With support from the Warshaw Pancreatic Cancer Research Institute at Mass General, the researchers used advanced digital gene analysis to study the RNA molecules of primary tumors. They first detected the massive presence of satellite repeats in a mouse model of pancreatic cancer, at more than 100 times the rate in normal tissue, with similar results in mouse colon and lung tumors—and in human pancreatic, prostate, lung, kidney and ovarian tumor cells.

“If confirmed in large prospective clinical trials, satellite RNA expression may provide a new and highly specific biomarker relevant to multiple types of epithelial cancers,” noted Cancer Center researcher David Ting, MD, who was primary investigator on the study.
New Portable Nuclear Imaging Device Promises Quicker, Accurate Cancer Detection

The Massachusetts General Hospital Center for Systems Biology has developed a portable device that delivers protein analysis of suspected cancer tumors to a physician’s smartphone. The micro-NMR (nuclear magnetic resonance) device uses magnetic nanoparticles to measure tumor proteins and other chemical compounds.

Using a combination of four cancer-related biomarkers, micro-NMR was found to have a 96 percent cancer detection accuracy rate. The research team led by Center for Systems Biology Director Ralph Weissleder MD, PhD, published its results in Science Translational Medicine in February.

New Targeted Drug Shows Promise Against Lung Tumors Driven by ALK Gene Mutation

Mass General Cancer Center investigators report that a new targeted therapy has demonstrated the ability to halt or reverse the growth of certain forms of non-small-cell lung cancer (NSCLC), the leading cause of cancer death in the United States. The study with eight other institutions has focused on tumors driven by fusion of the EML4 and ALK genes, a mutation characterizing 2 to 7 percent of non-small-cell lung cancers.

In the New England Journal of Medicine last October, researchers led by Jeffrey W. Clark, MD, and Eunice L. Kwak, MD, PhD, reported that crizotinib, an ALK and MET gene inhibitor, shrunk the tumors of more than half of the patients enrolled; it halted tumor growth in another third. The clinical trial is continuing, with research under way to develop the next generation of ALK inhibitors.

Cancer Center’s Gynecologic Oncology Team Advances Single-Incision Laparoscopy for Endometrial Cancer Patients

Surgical treatment of endometrial and other gynecologic cancers frequently involves the use of laparoscopic techniques, which have outcomes comparable to established methods, according to recent studies.

The use of single-incision laparoscopy (SIL), however, is relatively new. Reporting on their experience with this minimally invasive procedure in the Journal of the American College of Surgeons (JACS) in January, Mass General gynecologic oncologists David M. Boruta II, MD, Whifield B. Growdon, MD, and John O. Schorge, MD, FACS, said that the procedure’s benefits most notably include easier patient recovery, since it may require less narcotic analgesia, reduce instrumentation injuries and reduce risk of wound infection.

New Physicians Join the Cancer Center

Thirteen new physicians joined the Mass General Cancer Center in 2011. They include pancreatic and biliary surgeon Keith D. Lillemoe, MD, who is Mass General Hospital’s new Surgeon-In-Chief and Chief of the Department of Surgery, as well as:

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<tr>
<th>Clinical Area</th>
<th>HEMATOLOGY ONCOLOGY</th>
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<tr>
<td>Breast Cancer</td>
<td>Adriya Bardia, MD, MPH</td>
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<td>Breast Cancer</td>
<td>Amy H. Comander, MD, MA</td>
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<td>Gastrointestinal Cancers</td>
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<td>Gastrointestinal Cancers</td>
<td>Janet E. Murphy, MD</td>
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<td>Gynecologic Cancers</td>
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<td>Melanoma; Head and Neck Oncology</td>
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<td>UROLOGY</td>
<td>Genitourinary Cancers</td>
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<td>Christopher J. Cutie, MD</td>
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Cancer Center Online CME Offerings

The Mass General Cancer Center’s 2011 archive of Continuing Medical Education (CME) programs is available online through the Massachusetts General Hospital Academy (MGHacademy.org).

Users must register, then scroll down to access individual programs.

Online offerings include:

- Diagnosis and Management of GI Malignancies and Dysplasia
  February 1, 2011
- Management of Early Melanoma and Atypical Spitz Tumors
  February 17, 2011
- Management of Metastatic Melanoma
  February 17, 2011
- Care of the Elderly Patient with Leukemia
  April 2011
  Part I: Treatment of the Older Adult with Acute Myelogenous Leukemia
  Part II: Acute Myeloid Leukemia in the Elderly: Evaluating the Role of Allogeneic Stem Cell Transplantation

On-site offerings include:

- Hepatocellular Carcinoma: New Trends and Contemporary Management
  October 21, 2011
  Location: Simches Research Center, Massachusetts General Hospital
- Collaboration in Cancer Drug Trials: Targets, Biomarkers and Drugs
  Dates and Location TBA

For updated info visit: sto-online.org
# Selected Open Clinical Trials

The Massachusetts General Hospital Cancer Center conducts nearly 400 clinical trials in collaboration with the Dana-Farber/Harvard Cancer Center. Selected Mass General trials currently enrolling new cancer patients are listed here. For a complete list, go to: massgeneral.org/cancer/trials.

## Gynecologic Cancers

**09-286**  A Phase 2, Multicenter, Single-Arm Study Evaluating Carboplatin/Gemcitabine in Combination With BSI-201 in Patients with Platinum-Resistant Recurrent Ovarian Cancer  
Phase 2  
Michael J. Birrer, MD, PhD  
617-724-4800

## Head and Neck Cancers

**06-264**  A Phase 2 Clinical Trial of AZD2171 Monotherapy in Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma Patients  
Phase 2  
James W. Rocco, MD, PhD  
617-726-5251

## Hematology

**2009 P002612**  TMM-08: A Randomized Trial to Determine if There Is a Clinically Important Difference Between the Effect of Shorter Storage-Age RBCs vs. Longer Storage-Age RBCs on Clinical Outcome and Mortality Risk (RECESS)  
Phase 2  
Christopher P. Stowell, MD  
617-726-2815

## Leukemia

**07-006**  A Phase 1 Trial of Bortezomib in Combination With Lenalidomide in Patients with Myelodysplasia and Acute Myelogenous Leukemia  
Phase 1  
Karen Ballen, MD  
617-724-1124

## Lymphoma

**10-271**  A Phase 2 Trial of Ofatumumab for Initial Systemic Treatment of Indolent B-Cell Lymphomas  
Phase 2  
Jeremy S. Abramson, MD  
617-726-8743

## Melanoma

**10-056**  An Open-Label, Dose-Escalation, Phase 1 Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics and Clinical Activity of the BRAF Inhibitor GSK2118436 in Combination with the MEK Inhibitor GSK1120212 in Subjects with BRAF Mutant Metastatic Melanoma  
Phase 1  
Keith T. Flaherty, MD  
617-726-1941

## Multiple Myeloma

**10-203**  An Open-Label, Multicenter Study of AT7519M Alone and in Combination With Bortezomib in Patients with Previously Treated Multiple Myeloma  
Phase 1/2  
Noopur S. Raje, MD  
617-726-0711

## Neuro-Oncology

**09-468**  An Open-Label, Phase 2 Trial of Orally Administered PF-00299804 in Adult Patients with Relapsed/Recurrent Glioblastoma (GBM)  
Phase 2  
Andrew S. Chi, MD, PhD  
617-643-5530

## Pediatric Cancers

**09-273**  Reduced-Duration Stanford V Chemotherapy With or Without Low-Dose Tailored-Field Radiation Therapy for Favorable Risk Pediatric Hodgkin’s Lymphoma  
Phase 2  
Alison M. Friedmann, MD  
617-726-2737

## Sarcoma

**09-352**  A Phase 1/2 Study of PCI-24781 in Combination With Doxorubicin for Treatment of Advanced Sarcomas Following Failure of Prior Anthracycline Therapy  
Phase 1/2  
Edwin Choy, MD  
617-643-0230

## Targeted Therapeutics

**10-262**  A Phase 1A, Multicenter, Open-Label Dose Escalation Study of Oral BYL719, in Adult Patients with Advanced Solid Malignancies, Whose Tumors Have a Mutation of the PIK3CA Gene  
Phase 1  
Jose Baselga, MD, PhD  
617-726-2406

## Thoracic Cancers

**09-338**  A Phase 1-2 trial of MM-121 in Combination with Erlotinib in Three Groups of Patients With Non-Small-Cell Lung Cancer  
Phase 1/2  
Lecia V. Sequist, MD, MPH  
617-724-7829
especially those older than age 50, to tolerate a transplant. By switching to a regimen involving lower doses of drugs such as fludarabine and melphalan, and low-dose total body irradiation, Cancer Center physicians can now recommend stem cell transplants—including CBTs—for patients as old as 70. With the average age of a leukemia patient approaching 65, this reduced-intensity conditioning regimen extends the possibility of CBT and other stem cell transplants to many patients who previously were not eligible.

Selecting the Appropriate Cord Blood Unit

Dr. Ballen and her colleagues also are working to refine the criteria for an optimal cord blood transplant match. Many factors can influence the success of the transplant, including the degree of HLA match, the number of hematopoietic stem cells in the unit, and how the unit is processed. Preliminary results reaffirm the importance of HLA matching and cell dose. Patients with a less well-matched cord blood unit may benefit from a higher cell dose.

When the first cord blood transplant took place more than 20 years ago, the procedure was considered extremely high-risk. Now, with advances in HLA-matching, optimizing stem cell dose, and reducing posttransplant infection, CBT has become a viable treatment option for those patients who do not have a matched related or unrelated donor.

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The Importance of Public Cord Blood Banking

There is a critical need to extend the availability of cord blood transplantation (CBT), especially for minority patients, who have only a 10 to 20 percent chance of finding a suitable matched, unrelated donor among the standard transplant registries.

The American College of Obstetricians and Gynecologists, the American Academy of Pediatrics and the American Society of Blood and Bone Marrow Transplantation have released formal position statements strongly suggesting that parents donate their children’s cord blood to public banks. The only exception to this recommendation is if there is a first-degree relative with a disease or disorder, such as leukemia, which could be treated with CBT. In these cases, a private banking option may be preferable.

Physicians can help promote access to this critically needed cancer treatment method by educating their patients about the importance of public cord blood banking.

Selected References


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