Getting Personal

A new drug offers targeted therapy for cancer patients

Blocking the path
Seeking a second line of defense against HER2-positive breast cancer

The search for the source of serous ovarian cancers:

A medical detective story
Turning Point is published for supporters of Dana-Farber’s Women’s Cancers Program (WCP). To learn more about the WCP, call Administrative Director Candace S. Lowe, ScD, at 617-632-2675.

Comments, suggestions, and requests to be added to or deleted from the mailing list may be sent to:

Turning Point
Dana-Farber Cancer Institute
Department of Communications
44 Binney Street, OS300
Boston, MA 02115

or call 617-632-4090
or e-mail TurningPoint@dfci.harvard.edu

EDITOR: Michael Buller

SCIENCE ADVISORS: Ian Krop, MD, PhD,
Jennifer Ligibel, MD

ART DIRECTOR: John DiGianni

DESIGN: Lee Whale

CONTRIBUTORS: Christine Cleary, Robert Levy,
Pat McAffrey, Debra Bradley Ruder, Saul Wisnia

PRODUCTION: Jacqueline Czel

PHOTOGRAPHY: Sam Ogden

on the cover:
New Hampshire native Fermina Hanson is enrolled in an oral chemotherapy study at Dana-Farber.
Dana-Farber
Women’s Cancers Program

Through ongoing exploration into the molecular underpinnings of breast cancer and gynecologic cancers, researchers and clinicians at Dana-Farber Cancer Institute’s Women’s Cancers Program (WCP), are working together under the direction of J. Dirk Iglehart, MD, to shed light on the differences that define the many sub-types of these cancers that we now know exist. At the same time, researchers are looking to leverage the genetic similarities among different cancers to develop novel and increasingly effective therapies. One promising example is the discovery of a close genetic similarity between triple-negative breast cancer and serous ovarian cancer, a very fast-moving type of ovarian cancer. (See the article on page 12.)

The WCP’s many clinical trials (about 75 are open at any given time; see www.dana-farber.org/res/clinical/trials) give patients access to the latest treatments. For researchers and clinicians, these studies provide valuable insight into a treatment’s effectiveness. Many trials evaluate treatments prior to surgery and study the vulnerability of a specific cellular process, allowing oncologists to quickly determine the effectiveness of a drug or drug combination and someday make adjustments, if necessary.

WCP physicians and researchers continue to expand our growing knowledge of women’s cancers, through their own research and their close collaborations with colleagues at Harvard Medical School, and with leading institutions around the world. “The WCP hosts several clinical and research meetings each year,” says Dr. Iglehart. For example, Dana-Farber is a founding member of the Translational Breast Cancer Research Consortium, comprised of scientists from 16 academic medical centers around the country. The consortium started as a WCP-funded meeting of clinical researchers from across the country.

“Our physicians also present at and participate in leading national and international conferences to further the exchange of discoveries.”

For researchers and clinicians, these studies provide valuable insight into a treatment’s effectiveness.
Research in the Breast Cancer Program is progressing on multiple intersecting tracks. Studies aim to improve the effectiveness of current therapies, develop new agents for drug-resistant cancers, identify additional subtypes of tumors that respond to targeted treatments, uncover the biochemical signs of a tumor’s aggressiveness and vulnerability to therapy, and devise new approaches to cancer prevention and supportive care.

Women’s Cancers Program (WCP) investigators are leading and participating in an array of clinical trials of drugs for HER2-positive breast tumors that have become resistant to drugs such as trastuzumab (known also by the trade name Herceptin). Laboratory research by Dana-Farber scientists suggests that shutting down a protein called PI3 kinase – which may be active in trastuzumab-resistant, HER2-positive tumors – can lead to cancer cell death. Institute investigators are studying the safety and effectiveness of several PI3 kinase blockers in patients.

Many research projects are focused on women with metastatic breast cancer. WCP investigators have launched studies of drugs that may act against breast tumor cells that have spread to the brain, a site of metastasis that represents a particular challenge.

A variety of investigations center on triple-negative breast cancers, so called because they don’t respond to hormonal treatment or HER2-directed therapy, such as trastuzumab (Herceptin). An approach to drug resistance is being explored in clinical trials of agents known as PARP inhibitors, which can block the ability of cancer cells to sustain themselves by repairing their own DNA.

Investigators have also widened their focus from a concern with cancer cells themselves to a consideration of the interactions of tumor cells with surrounding, healthy tissue. WCP investigators have shown that the ability of tumor cells to disrupt the normal development of milk duct cells enables the tumor cells to escape the ducts and travel to other parts of the body.

Critical to the success of this work is access to tissue from patients. The Lurie Breast Cancer Tissue and Translation Initiative has enabled Dana-Farber investigators to bank blood samples from thousands of breast cancer patients. This resource is complemented by the breast tumor tissue bank at Brigham and Women’s Hospital. This bank was begun in 2000 using funds from the WCP and now houses breast cancer samples from more than 1,400 patients. Tissue stored in these facilities is used in studies to uncover cancer-related gene mutations or identify proteins in the blood that signal the presence of early cancer.

In late 2008, investigators launched a new study that will follow women with metastatic breast cancer over several years. Over that time, they will be able to obtain serial blood samples and tumor specimens that will give researchers the valuable data and tissue needed to help further our understanding of the molecular changes that take place in metastatic breast cancer. The important study, which is currently enrolling patients, is made possible because of a generous gift from Karen Webster and David Evans.

Physicians within the WCP have uncovered significant disparities in the extent of breast cancer treatment received by women of different racial and ethnic groups. Those findings are a starting point for studies of the underlying reasons for the disparities, and for efforts to ensure that all patients receive equally thorough treatment programs. Other studies focus on the physical and psychological effects of breast cancer treatment in young women.
Research into the basic biology of gynecologic cancers – including those of the ovary, cervix, uterus, and vulva – is bringing into focus an array of new approaches to therapy. Investigators probing ovarian cancer are hoping to identify precursor (precancerous) cells for this particularly challenging disease, so it can be stopped before it develops. Warning signs like bloating, pelvic/abdominal pain, and urinary urgency or frequency usually don't emerge until cancerous tumors have grown or spread. At this advanced stage, the disease can be very difficult to treat successfully.

In one project under way at the Dana-Farber/Brigham and Women's Cancer Center (DF/BWCC), researchers led by Christopher Crum, MD, have shown that some ovarian tumors initially arise in the fallopian tubes and secondarily spread to the ovaries and peritoneum. This remarkable result was proven by tracking a single mutation in a gene called p53 from the earliest cells in the fallopian tube to advanced cancer in the pelvis. If overexpression of this gene turns out to be a direct link to ovarian cancer, there is a chance the disease could be detected – and thwarted – much earlier on. (For a detailed story on the p53 mutation, see page 12.)

“We need to find some kind of definite precursor for ovarian cancer, like polyps are for colon cancer or DCIS (ductal carcinoma in situ, a precancerous condition in which abnormal cells grow in the milk ducts) has become for breast cancer,” says Ursula Matulonis, MD, director of Gynecologic Medical Oncology for Dana-Farber's Women's Cancers Program. “If you find and stop the source, you can better stop the cancer. I'm confident that's where we're headed.”

In another effort, for which Dana-Farber received a Breast Cancer Research Foundation grant last year, DF/BWCC physicians including Dr. Matulonis, Ross Berkowitz, MD, and Charles Wang, MD, PhD, are comparing the genetic makeup of triple-negative breast cancer (a particularly aggressive form) and ovarian cancer. Their work is part of an attempt to understand the molecular similarities and dissimilarities between these two diseases, which are both very sensitive to platinum-based drugs often used for cancer treatment.

Beyond ovarian

Another area of increasing interest is uterine cancer – the fastest-growing gynecological cancer in the United States, with about 40,000 new cases each year. Obesity can drive up estrogen levels in the blood, which in turn can fuel endometrial growth and raise the risk of uterine cancer. One promising study is being led by Heidi Greulich, PhD, of Dana-Farber and the Broad Institute of Harvard and MIT, who is investigating the genetic makeup of endometrial cancer.

On the cervical cancer front, Dorre Gruenberg, PhD, of Harvard Medical School and the Broad Institute is leading investigations into the role a particular kinase (an enzyme that serves as a switch for genetic activity) may play in tumor cell growth. And in vulvar cancer, Neil Horowitz, MD, is heading up a promising clinical trial studying how a deadly abnormal gene known as EGFR (epidermal growth factor receptor) can be stopped with molecularly-targeted therapies.
Just as the role of genetics in determining cancer risk has become more widely understood in recent years, so too has Dana-Farber widened its knowledge – and its services to help a growing number of people assess and manage their risk of passing down or developing the disease.

When the Friends of Dana-Farber Cancer Risk and Prevention Clinic (CRPC) first opened its doors, there was one medical oncologist and one genetic counselor on staff. The clinic saw about 400 patients and family members that year. Under the leadership of Director Judy Garber, MD, MPH, the CRPC has expanded to include four physicians and seven genetic counselors who last year offered personal risk assessment, genetic counseling, screening evaluations, and strategies to reduce cancer risk to approximately 1,500 patients and families.

The clinic now offers a full range of services at both its main facility in Boston’s Longwood Medical area as well as at satellite centers at Faulkner Hospital in Jamaica Plain and at new centers in Milford, Mass., and in Londonderry, N.H.

The CRPC’s impact is also measured in our growing understanding of women’s risk of developing ovarian and breast cancer, and the prevention and treatment strategies associated with each.

“It’s one thing to talk with people about their risk, and it’s another thing to try to help them deal with it,” says Dr. Garber. “We don’t just do the assessment. We follow these patients. We manage them. We care for them, and for their families.”

While all women are at risk, women with a family history of breast cancer in close relatives of young ages have a greater probability of developing one or both diseases over their lifetimes. About 10 percent of breast cancers are hereditary, and, of these, mutations in two genes, BRCA1 and BRCA2, are responsible for approximately 40 percent of the diagnoses. Women who have alterations in either of these genes have a lifetime risk of developing breast cancers between 55 percent to 85 percent, and a similar risk of developing a deadly ovarian cancer. With this understanding, the Risk and Prevention Clinic can tailor strategies to help women manage that risk.

Multiple studies at the clinic are examining ways to reduce both the threat of breast cancer in higher-risk women and the complex psychosocial issues related to harboring a susceptibility gene and undergoing genetic testing. One large study involves a drug known as a PARP inhibitor, which has been shown to prevent mammary tumors in mice without functional BRCA1 or BRCA2 genes. While it is important that these agents first be fully evaluated for safety in breast cancer patients, the findings suggest that PARP inhibitors could form the basis for effective prevention strategies for women with inherited breast cancer risk. Additional research is also studying the potential of PARP inhibitors in treating women with advanced ovarian cancer. (See article on page 16.)

Dr. Garber and others at the center are also working with Dana-Farber colleague Jennifer Ligibel, MD, to examine the effects of exercise on reducing cancer risk. (See article on page 7.)

Looking even further into the future, Dr. Garber can envision a day when a breast cancer gene test will screen for a larger percentage of diseases, help identify at-risk women, and guide cancer prevention strategies. Dr. Garber says, “This is true of heart disease already, and, in many ways, it’s what you hope for in cancer.”
Vulnerability, or the theory that all cancer cells have at least one weakness, is a concept embraced by much of the cancer research field. This theory holds that you beat cancer by finding the molecular Achilles’ heel of particular cancer cells and designing drugs that interfere with this particularly vulnerable spot. This approach is just one of the ways in which Dana-Farber scientists are pursuing a multi-front attack on women’s cancers. Increasingly, that battle focuses on the complex interactions within specific types of tumor cells that allow them to proliferate and sometimes spread to other areas of the body.

The use of the drug trastuzumab (Herceptin) to treat women with HER2-positive breast cancer, for example, has significantly improved the lives of many patients. But in time, the tumors of some patients become resistant to the drug. Scientists believe that the PI3 kinase plays a critical role in this process. Like all kinases, the PI3 kinase acts as a switch box in the cell’s communication network. In these trastuzumab-resistant tumors, PI3 kinase may provide an alternate pathway that allows tumor cells to survive. A Women’s Cancers Program (WCP) clinical trial, headed by Ian Krop, MD, PhD, is studying the effectiveness of a PI3-kinase inhibitor in shutting down the pathway. (See the article on page 16.)

The article on page 12 provides another example of our growing understanding of the genetic underpinnings of cancer. That story details the findings of Christopher Crum, MD – that many serous ovarian cancers may actually begin in the fallopian tube rather than the ovary – and the work of other WCP researchers to confirm his findings.

From discoveries of the mechanisms of DNA repair and drug resistance, to the search for biomarkers that aid in early detection of the disease, to gene mutations that raise the risk of developing cancer, research from the WCP continues to advance our understanding of the fundamental processes within tumor cells, and lead us toward more effective and less toxic treatments for breast and gynecologic cancer patients.
**Ask the Care Team**

**What is the HPV vaccine? Who should receive it? And what are the associated side effects?**

The vaccine for HPV (or human papilloma virus) is highly effective in preventing infection in women who have not previously been infected with two particular viruses – called HPV 16 and 18 – covered by the vaccine. However, there are several other HPV subtypes that are not covered by the current vaccine. It does not prevent the majority of infections and abnormal growths caused by these other viruses, nor does it protect patients who have already been infected with HPV 16 or 18. We also don't know for how long women who receive the vaccine will be protected.

The main side effect is pain at the injection site and there have been some news reports about other serious side effects. There is a system for reporting adverse events, and to our knowledge those other complications have not been confirmed as being caused by the vaccine.

The vaccine does not change the recommendations for having a routine Pap test. The HPV vaccine protects against only two of 13 high-risk viral subtypes, but even with those two types, it cannot prevent further consequences of pre-existing infections. A Pap test is a screening test that looks for cellular changes associated with HPV infection. Pap testing remains the best method for detecting precancerous changes. All women should continue following standard screening practices. Otherwise, their risk of cervical cancer could actually rise. Ultimately, a combination of an expanded vaccine and more specific viral testing may change how we screen for cervical cancer, but we're not there yet.

**What are biomarkers and how are they affecting diagnosis and treatment of ovarian cancer?**

A biomarker is a biochemical feature, usually a protein in a biological fluid (blood, serum, urine, saliva) that can be used to measure the progress of disease or the effects of treatment.

There are two FDA-approved biomarker tests (both blood tests) for ovarian cancer: CA125 and HE4. Both are approved for assessing the response to initial chemotherapy following diagnosis.

CA125, discovered at Dana-Farber/Brigham and Women's Cancer Center, is the most studied and widely used ovarian cancer biomarker. Although it plays a major role in monitoring patients, CA125 alone is not good for early detection because it can be triggered by numerous benign conditions.

Ongoing studies are trying to address the use of HE4 as a new tool to help doctors determine the most appropriate course of care for women with a pelvic mass, and as a biomarker for early detection of the cancer.

**What is uterine cancer and what are the risk factors for uterine cancer?**

Uterine cancer is a malignancy that develops in the lining of the uterus, in the hormone sensitive tissues that nourish a newly implanted embryo and that slough off monthly during the menstrual cycle. This tissue is called the endometrium, and the cancer may be called “endometrial cancer.” Uterine cancer typically presents itself as abnormal vaginal bleeding or spotting when it is small, and as an enlargement of the uterus when it is advanced. It is diagnosed by an endometrial biopsy, done in the office, or by dilation and curretage (“D and C”) in the hospital. It is treated by surgery (hysterectomy), sometimes with radiation, and sometimes with hormones and chemotherapy.

Risk factors for uterine cancer are both genetic (inherited) and non-genetic, and in the categories of lifestyle and environmental factors. Inherited deficiencies in a class of DNA repair enzymes called “mismatch repair” enzymes can cause gastrointestinal cancers (e.g., colon and stomach) and cancer of the uterus. Taking estrogen without taking progesterone after menopause is a risk factor for uterine cancer, and the reason why all “hormone replacements” are given as combinations of estrogen and progesterone unless a woman has previously undergone a hysterectomy. Finally, obesity and lack of exercise seem to put post-menopausal women at risk for uterine cancer, probably by increasing the exposure to estrogen without the benefit of progesterone.
Exercise shown to lower insulin in breast cancer survivors

Through observational studies, doctors and scientists have known that women who engage in even a modest amount of physical activity after breast cancer diagnosis appear to have a lower risk of cancer recurrence than inactive patients. Now, a randomized clinical trial led by Jennifer Ligibel, MD, of Dana-Farber’s Breast Oncology Center, suggests that the protective effect of increased fitness may result from lowering insulin levels in the body.

A report published in the February 2008 issue of the Journal of Clinical Oncology showed that moderate exercise such as walking, along with supervised strength training sessions, led to a 30 percent decrease in levels of insulin in previously sedentary breast cancer survivors.

“While other types of studies are based on the composition of the tumor, our research is a little different because we focus on the characteristics of the [patient],” Dr. Ligibel points out. “We ask which factors, such as inactivity, set the stage for breast cancer to thrive or come back.”

No one knows if increased fitness will prevent breast cancer recurrence, but the women improved their overall health. Dr. Ligibel and her colleagues learned the value of a supervised exercise program: “Fitness is all about motivation,” she says. “Women are more likely to exercise when enrolled in a program with frequent check-ins.”

The study lays the groundwork for further experiments. Dr. Ligibel is leading several other trials at Dana-Farber related to exercise and breast cancer. One trial looks at the potential benefits of exercise in women living with metastatic breast cancer. Another trial is evaluating the ability of a telephone-based exercise program to increase physical activity in survivors of breast or colorectal cancer. “Our hope is that one day, our ongoing research will shed more light on the value of exercise as a standard component in breast cancer treatment,” she says.

Finding open clinical trials

At Dana-Farber, there are hundreds of research studies going on as investigators attempt to better understand the diseases. You can learn about clinical trials through Dana-Farber’s Web site at www.dana-farber.org/res/clinical, which lists all open trials by diagnosis, or by calling 866-790-4500. All Dana-Farber trials are open to current patients or those thinking about coming to the Institute.

Some studies allow individuals who have not been diagnosed with cancer to participate. Healthy volunteers may serve as a comparison group in studying how chemotherapy and other treatments affect the body.
Genes may hold vulvar cancer clues

If Neil Horowitz, MD, wants extra motivation to continue the work on vulvar cancer that he and his colleagues at Dana-Farber/Brigham and Women's Cancer Center are undertaking, he need look no further than his e-mail inbox. Every month, Dr. Horowitz gets e-mails from people all over the world interested in joining clinical trials for this relatively rare disease, which is diagnosed in only 3,000 patients each year in the U.S.

Cancer of the vulva, the outer part of a woman's genital organs, typically presents with signs like itching, tenderness, and non-menstrual bleeding. Fortunately, it is often diagnosed when still confined to the vulva, in which case it carries a five-year survival rate of 90 percent. However, in three out of every 10 cases, the cancer can spread to the lymph nodes. When this happens, survival drops to 50-60 percent. In such cases, recurrence rates are high and survival after recurrence is poor.

Clinical trials led by Dr. Horowitz and others are aimed at thwarting vulvar cancer by suppressing the genes and proteins responsible for it. “Our early response rate has been very encouraging,” he says of one study now underway at Dana-Farber. “A genetic fingerprint called EGFR [epidermal growth factor receptor] is heightened in many vulvar cancer patients, and we’re hoping that giving them a drug called Tarceva, or erlotnib, can block the receptor and its downstream growth signals to shrink existing tumors. This is especially encouraging for patients with recurrent disease who have few options for treatment, or for those in whom radical surgery can be disfiguring and negatively impact bodily function.”

Dr. Horowitz says two groups account for most vulvar cancer cases: younger women who smoke and have the human papilloma virus (HPV), and older women who have a long history of chronic vulvar irritation. The key will be uncovering which group or subset therein best responds to Tarceva, and then targeting it to them. The drug has already proven effective in treating some advanced small-cell lung cancer patients.

Targeting a tumor’s repair mechanism

Along with surgery and chemotherapy, radiation therapy has been a mainstay of cancer treatment almost since X-rays were discovered in 1895. High-energy beams of radiation attack rapidly dividing – and therefore vulnerable – cancer cells by scrambling their DNA blueprints, halting their growth, and shrinking the tumor.

Technology has continuously improved so that higher doses of radiation can be delivered more accurately, hitting cancers harder while sparing normal tissues. At the same time, scientists in Dana-Farber’s Department of Radiation Oncology are exploiting defects in cancer cells’ defenses – weakening their ability to repair DNA damage so tumors can’t rebound after being treated with radiation therapy.

“Tumors become resistant by repairing the DNA damage to their cells,” explains Dana-Farber’s Alan D’Andrea, MD. The repair work is done by turning on one or more of six different molecular pathways that specialize in repairing damaged DNA. “If you can determine which pathways are active in a patient’s tumor, you can predict its sensitivity to particular types of radiation or chemotherapy,” Dr. D’Andrea says. Research suggests that it may be possible to “throw a wrench” into the repair mechanisms and prevent the tumor from healing itself.

Dr. D’Andrea heads the Division of Genome Stability and DNA Repair within the Department of Radiation Oncology, which is developing various methods to pinpoint which DNA repair pathways are active in a patient’s tumor. These “snapshots” of pathway activity help guide therapy. In many cases, cancer cells shut down a major repair pathway so that they are more prone to mutation and can evolve resistance to therapies more rapidly. The trade-off is that they become more dependent on other pathways. If scientists can knock out one of the remaining dominant repair pathway, radiation or chemotherapy has a greater chance of striking a lethal blow.

Dana-Farber’s Larissa Lee, MD, and collaborators at Beth Israel Deaconess Medical Center are studying a database that includes information on the outcomes of treated breast cancer patients, along with data on molecular studies of their tumor tissue. Some of those tissue samples have been “profiled” to identify the most active DNA repair pathways in the tumor.

“We want to match the profiles with patients who’ve done well for a long time, and those who have had recurrences, to see if these biomarkers (indications of repair pathway activity) can predict who is more likely to have a recurrence,” says Dr. Lee.

Jay Harris, MD, chair of the Dana-Farber Department of Radiation Oncology, says, “This research may open opportunities to tweak DNA repair pathways in a way that enhances the effect of radiation therapy, increasing the kill of tumor cells as well as protecting normal tissues.”
In about 20 percent of breast cancer cases, the tumor cells have an oversupply of a protein called HER2. For women with such “HER2-positive” tumors, trastuzumab can literally be a lifesaver. By binding to HER2, the drug prevents it from transmitting growth signals into the cell, slowing or reversing tumor growth. Combined with chemotherapy, the drug shrinks or controls tumors in 75-80 percent of women with HER2-positive metastatic breast cancer.

Even in these patients, however, the benefits of trastuzumab are far from permanent. Patients with the most advanced disease generally have a 10- to 14-month period in which their condition improves or stays stable, after which it begins to worsen, although some patients do well for many years.

“It’s as though HER2-positive cancers are speeding down a highway. Trastuzumab cuts them off for a while, but the tumors have a way of finding off-ramps that enable them to get around the blockade,” says Eric Winer, MD, director of the Breast Oncology Center within Dana-Farber’s Women's Cancers Program (WCP). “There’s a growing scientific and clinical consensus that even when the cancer progresses, Herceptin is still providing a benefit, so the drug resistance is only partial.

“We’re beginning to understand what’s taking place at a molecular level to enable these tumors to escape the full effect of the drug,” he continues. “What’s exciting is that there are a host of drugs in preliminary clinical trials that appear to have very clear activity against Herceptin-resistant cancers.” (See box on page 11 for a brief description of these studies.)

**Molecular maneuvers**

Scientists have discovered that when HER2-positive breast cancer cells become resistant to trastuzumab, proteins called PI3 kinases become activated within the cells. The
In about 20 percent of breast cancer cases, the tumor cells have an oversupply of a protein called HER2. For women with such “HER2-positive” tumors, trastuzumab can literally be a lifesaver. By binding to HER2, the drug prevents it from transmitting growth signals into the cell, slowing or reversing tumor growth. Combined with chemotherapy, the drug shrinks or controls tumors in 75-80 percent of women with HER2-positive metastatic breast cancer.

Even in these patients, however, the benefits of trastuzumab are far from permanent. Patients with the most advanced disease generally have a 10- to 14-month period in which their condition improves or stays stable, after which it begins to worsen, although some patients do well for many years.

“It’s as though HER2-positive cancers are speeding down a highway. Trastuzumab cuts them off for a while, but the tumors have a way of finding off-ramps that enable them to get around the blockade,” says Eric Winer, MD, director of the Breast Oncology Center within Dana-Farber’s Women’s Cancers Program (WCP). “There’s a growing scientific and clinical consensus that even when the cancer progresses, Herceptin is still providing a benefit, so the drug resistance is only partial.

“We’re beginning to understand what’s taking place at a molecular level to enable these tumors to escape the full effect of the drug,” he continues. “What’s exciting is that there are a host of drugs in preliminary clinical trials that appear to have very clear activity against Herceptin-resistant cancers.” (See box on page 11 for a brief description of these studies.)

**Molecular maneuvers**

Scientists have discovered that when HER2-positive breast cancer cells become resistant to trastuzumab, proteins called PI3 kinases become activated within the cells. The kinases are a family of enzymes – proteins that spark chemical reactions – first studied by Thomas Roberts, PhD, co-chair of Dana-Farber’s Department of Cancer Biology, and Lewis Cantley, PhD, of Beth Israel Deaconess Medical Center and a member of the Dana-Farber/Harvard Cancer Center.

The PI3 kinases usually take their cues from the HER2 protein. HER2 is a “receptor” that juts from the cell surface like a catcher’s mitt waiting for a growth molecule. The “grow” command is passed along a chain of proteins, including PI3 kinases, to the cell’s central command. When HER2 is shut down by trastuzumab, abnormal PI3 kinases can sometimes
To learn whether breast cancers leave telltale signs of themselves in the bloodstream, researchers need to examine samples of tumor tissue—several thousand of them, ideally.

Ian Krop, MD, PhD, and Deborah Dillon, MD, of Dana-Farber/Brigham and Women’s Cancer Center are working to create just such a repository for Women’s Cancers Program scientists. With tumor tissue from current and former breast cancer patients, the bank will assist the search for cancer biomarkers—proteins and other substances in the blood that can reveal whether a tumor has formed and whether a therapy is effective.

Researchers will be able to divide the samples into distinct categories to identify biomarkers associated with each type. “We’d like to study reasonably uniform cohorts of patients who have received similar treatments,” says Dr. Krop. “By examining large numbers of samples, we can have confidence that our findings will be broadly applicable to each group of patients.”

The project involves a sizable commitment of effort and funds. Systems need to be put in place for collecting tumor tissue shortly after surgical removal, preserving it, staining it to show possible biomarkers, and cross-linking the data with patients’ medical history. The rewards, both in terms of improved tumor detection and more rapid development of treatments, promise to be substantial.
A top every list of how to deal with cancer is the importance of early detection. Regular screenings – self exams and those conducted by clinicians – are the surest way of detecting tumors in their initial stages, when they’re easiest to treat.

For nearly every type of cancer, that advice is perfectly sound. Cancer is like a brush fire, best stamped out or contained when it first forms, before it has a chance to spread.

But there are some cancers that don’t have a known formative stage, that seem to burst onto the scene in an advanced, malignant state, having already overrun a wide swath of tissue. Such tumors are notoriously difficult to treat, their sudden emergence a sign of their ferocity.

One of the most common of these tumors is known as serous ovarian cancer. Less than a quarter of the cases are detected at an early stage, a figure reflected in the survival rates for the disease.

Serous cancers occur on the surface of the ovaries and surrounding membranes, often in several places, making them impossible to eliminate by surgery alone. The introduction of drugs like platinum and taxanes have lengthened the survival of many patients, but cure rates have not substantially improved.

“When these cancers are diagnosed they seem to be everywhere at once,” says Ronny Drapkin, MD, PhD, of Dana-Farber’s Women’s Cancers Program (WCP), who is leading some of the research into the tumors’ origins. “Their discovery at an advanced state of development limits our ability to treat them effectively. That’s why it’s so important to identify ‘precursor’ cells from which the tumors arise.”

Cancer, in a nutshell

Over the course of modern cancer research, scientists have mapped out what might be called “The Genesis of a Cancer,” the step-by-step process by which some tumors form in the lining – or “epithelial” layer – of tissues and organs. It begins with a completely normal cell, anywhere in the body, whose DNA is damaged by exposure to a chemical, radiation, or the normal stresses of life. The cell then may repair the damage or kill itself to prevent the defect from being passed on to its offspring. If the damage is not repaired and occurs in a gene responsible for cell growth and division, the cell may be a cancer precursor, behaving oddly in one or two respects, but not immediately dangerous. Only after it acquires additional damage, or genetic mutations, does it acquire the classic characteristics of cancer – proliferation, burrowing into tissue, siphoning blood and nutrients from other cells, refusing to die on time, and demonstrating an ability to spread to other parts of the body.

This process means that scientists should be able to identify a continuum for the development of virtually any tumor they come across – the normal tissue where it originated, the quirky precursor cells that follow, the invasive and restless cells that mark it as cancer. In the case of high-grade serous ovarian cancer, however, the trail has been cold: for years, scientists couldn’t find a trace of the cells that preceded full-blown tumors.

“We had to ask ourselves whether this disease is a
detective story

Ronny Drapkin, MD, PhD, and his team direct the “living” bank of ovarian tumor tissue at Dana-Farber.
fondly different entity from other types of cancer, or whether we had been looking for precursor cells in the wrong place all along,” says Christopher Crum, MD, director of women’s and perinatal pathology at Dana-Farber/Brigham and Women’s Cancer Center (DF/BWCC), who sought to unravel the mystery of the condition’s origins.

‘Carpetbagger’ cancers
A key clue lay outside the ovaries themselves. The fallopian tubes, the narrow chutes that carry fertilized eggs to the uterus, also can be the site of origin of serous cancers. Can advanced serous cancers of the ovary actually be decoys – the result of cancer cells that left the fallopian tubes and settled in the ovary?

The evidence is pointing in that direction. First, the ovary and fallopian tubes are next-door neighbors – the broad end of the fallopian tube cupping the ovary in finger-like strands called fimbra – so cancer cells don’t have to travel far to go from one to the other. Second, ovarian and fallopian tube cancer cells look identical under a pathologist’s microscope and behave quite similarly.

If high-grade serous ovarian cancers (HGSOCs) are in fact masquerading fallopian tube tumors, then women diagnosed with HGSOC would be likely to have cancerous lesions, or sections of diseased tissue, on their tubes. Traditionally, however, pathologists haven’t examined the entire fallopian tube, concentrating on the more accessible central section of the tube.

In 2005, Dr. Crum and his colleagues developed a special technique for inspecting the “fimbriated” end of fallopian tubes – the portion, adjacent to the ovaries, with slender tendrils like the top of a sea anemone. Using this technique, called SEE-FIM (for “Sectioning and Extensively Examining the Fimbriated end”), they conducted a top-to-bottom exam of fallopian tubes that had been removed as a preventive measure from women with an inherited risk for ovarian cancer.

In a succession of studies, Dr. Crum’s team found that some of the tubes harbored early cancers, almost always in the fimbriated end, the end closest to the ovary. “This was strong evidence that the source of many serous carcinomas in the pelvic region, including the ovary, is the fimbriated – or ‘distal’ – end of the fallopian tube,” Dr. Crum says. “These are tumors that seem to grow best outside their birthplace.”

The evidence may have been strong, but it wasn’t yet definitive. Then, in 2006, Dana-Farber’s Alexander Miron, PhD, used advanced gene-sequencing technology to show that the early cancers in the fallopian tube had the same genetic mutations as the tumors elsewhere in the pelvis.

In search of precursors
Having found the fallopian tubes to be the “nursery” of many high-grade serous ovarian cancers, researchers could focus on their ultimate quarry, figuring out how and where normal cells become precancer and then cancer.

Here, a surprise was in store. Studies had shown that early cancers in the lining of the fallopian tube contain high levels of a protein called p53. The accumulation of the protein, caused by a breakdown in the p53 gene, was dubbed “the p53 signature.” When Dana-Farber and Brigham and Women’s
researchers tested normal-looking fallopian tissues, they found that about half the samples also had the p53 signature.

“That was the ‘Wow’ moment,” Dr. Crum says. “We now had a marker for these types of serous cancers and a pathway by which they develop: normal cells acquire mutations in the p53 gene, further mutations produce cancers within the fimbrial tissue of the fallopian tube, and the cancers migrate to the ovary.”

The discovery doesn’t imply that every woman whose fallopian tubes carry the p53 signature will develop serous cancers: in fact, only a small percentage of them will. But it has enabled scientists to construct a narrative about how such cancers arise and spread, and how they might be stopped.

Every month when women are menstruating, an egg pops out of an ovary in what has been described as a “mini explosion.” The tear in the ovary is mended by a blend of hormones and other proteins from the immune system. On rare occasions, this fix-it crew may inadvertently meddle with the DNA in nearby cells, such as those in the fimbriated ends of the fallopian tubes. One gene that’s susceptible to such changes is p53, whose job is to repair damaged DNA. A mutation can render the p53 protein useless, leaving the cell vulnerable to further mutations that could make it cancerous. The mutation also causes p53 to loiter too long within the cell – hence the p53 signature in precancerous cells.

“The p53 signature is like a sign telling us that the cell’s self-repair system is down,” Dr. Crum says. If this theory is correct, then women who have fewer children and have children at an older age – and thereby have a higher lifetime number of menstrual cycles – would be more likely to develop precancerous cells. Research by Dr. Crum, in association with Judy Garber, MD, MPH, director of the Friends of Dana-Farber Cancer Risk and Prevention Clinic, and Shelley Tworoger, PhD, an epidemiologist at Brigham and Women’s Hospital (BWH), found this to be the case.

As for why serous cancers often take root in the ovary rather than their “native soil” in the fallopian tube, scientists speculate that the ovarian terrain is somehow more hospitable for the fledgling tumor cells.

**Future directions**

Knowing the ultimate source of many serous ovarian tumors raises some intriguing possibilities for treatment. Understanding how precancerous cells become cancerous may suggest ways of disrupting the process before malignancies develop. Being able to detect cancers in their earliest stages – or identify tissue where tumors are likely to form – could dramatically raise survival rates for the disease.

WCP researchers have assembled a team with the expertise to reach those goals. The team includes Dr. Drapkin and his colleagues who are developing model systems of fallopian tube cells and their precancerous descendents; Dr. Miron, who conducts genetic analyses of cell and tissue samples; Dr. Crum, who heads the pathology efforts; Dr. Garber, who studies cancer risk factors; Tan Ince, MD, PhD, of BWH, who directs a live cell bank; Ross Berkowitz, MD, director of Gynecology and Gynecologic Oncology at BWH and Dana-Farber, Ursula Matulonis, MD, director of Gynecologic Medical Oncology at Dana-Farber, and Michael Muto, MD, and Colleen Feltmate, MD, of the Gynecologic Oncology program at DF/BWCC, who treat patients and lead clinical trials of new therapies.

“The pieces are in place, both technological and scientific, to get a handle on the development of serous cancers of the ovary, and to use those abilities to design and test more effective treatments,” Dr. Drapkin remarks. “We’re in a position to bring treatment of this disease into the age of targeted therapies.”
When Fermina Hanson needed to have chemotherapy and radiation for her breast cancer, one side effect really got her down. It wasn’t the nausea or fatigue, although both were debilitating. The thing she remembers most was the psychological impact of losing her long, dark hair. “It was traumatic, and a real struggle,” Hanson recalls.

Targeted therapy takes aim at breast and ovarian cancers

by Pat McCaffrey
Back on therapy for a recurrence of her cancer, the 54-year old Hanson is having a different experience this time. For the last eight months, she has been taking an experimental drug called a PARP inhibitor. [PARP stands for poly (ADP-ribose) polymerase.] A PARP inhibitor is a new, targeted therapy for breast and ovarian cancer that is being tested at Dana-Farber. Her treatment consists of eight pills, twice a day. Her tumor has receded. Her hair looks great.

Targeted therapies, such as PARP inhibitors, are designed to zero in on the exact genetic changes that make cancer cells so deadly, and leave normal cells alone. That lets the treatment effectively kill tumors and spare patients from the severe side effects that often come with chemotherapy. For Hanson, whose cancer is caused by a mutation in one of the two most common breast cancer genes (BRCA1 and BRCA2), the PARP inhibitors offer the first potential treatment aimed at hereditary breast cancer. That is good news for the approximately five percent of breast and ovarian cancer patients with BRCA mutations. For other women, new research points to a similar defect even in tumors without BRCA mutations, and opens the door to the possibility that PARP inhibitors could be effective against a wider range of both ovarian and breast cancers.

Six ways to fix DNA

Research into BRCA function over the past decade, including key work by scientists in Dana-Farber’s Women’s Cancers Program, elucidated the role of BRCA proteins involved in DNA repair. Researchers have identified six different repair mechanisms (or pathways), each made up of dozens of proteins that work together to mend breaks and correct genetic mistakes. This process is critical to cell life; without it, cells quickly accumulate a lethal load of genetic damage.

In breast and ovarian cancers with BRCA mutations, one of the six repair pathways loses function. To survive, the cells compensate by increasing the activity of an alternative repair pathway. The PARP enzyme is a key protein in the back-up pathway, and the tumors soon become dependent on PARP activity for their survival.

Once the biology of PARP in BRCA-deficient cells became clear, clinical translation quickly followed. PARP-inhibiting compounds were already sitting on the shelf at several pharmaceutical companies, the product of earlier investigations for other disease treatments. So far, the results from clinical trials in cancer patients have been encouraging.

In the Gynecologic Medical Oncology Program, Director Ursula Matulonis, MD, and her team have completed a first study of the PARP inhibitor AZD2281. All of the women who took part had recurrent ovarian cancer and the BRCA1 or BRCA2 mutations; they all received the PARP inhibitor, and though the study was small, the doctors saw some “remarkable” responses. “PARP inhibitors are definitely active drugs in these patients,” Dr. Matulonis said.

Doctors are now recruiting for a follow-on study comparing the same PARP inhibitor to a standard treatment regimen in women with advanced ovarian cancer whose cancer progressed in spite of prior chemotherapy.

Fermina Hanson had her first bout with breast cancer in 1997. When the tumor reappeared in 2004, she came to see Harold Burstein, MD, PhD, at Dana-Farber’s Breast Oncology Center. She received a standard course of radiation and chemotherapy for her BRCA2-positive tumor. Two years later, after another local recurrence, Dr. Burstein suggested a clinical trial. The first experimental treatment she tried had no effect, but she then enrolled in a multi-center study of PARP inhibitors and she’s seen her tumor shrink.

When she was undergoing chemotherapy and radiation, Hanson traveled to Dana-Farber at least weekly from her home in Brookline, New Hampshire, and had to take a leave from her job as a medical secretary when the side effects became too severe. With the PARP inhibitor, she takes her pills in the morning and evening, feels a little tired and sometimes nauseous, but she says, “I go to work, I do everything I want to do. To have a drug with so few side effects and that is effective, is wonderful.”

“This is a very new drug, and I know there aren’t that many people on it worldwide. But my background matched it, and now I’m having positive results,” Hanson said. “A big reason I chose to go to Dana-Farber is because they have these opportunities for study drugs. I feel blessed to have this chance.”

Not for BRCA cells only?

Only a fraction of women with breast and ovarian cancer have BRCA mutations, but many tumors have
defects in DNA repair. In ovarian cancer, up to 70 percent of tumors are deficient in some part of the the BRCA DNA repair pathway, even though their BRCA genes may be normal. The problem could lie in regulation of BRCA gene expression or in trouble with other proteins in the same pathway. Whatever the cause, if the cells are relying on the PARP pathway to take up the slack, the inhibitor might work for these tumors, too.

To test that idea, Dr. Matulonis is planning a trial to evaluate the compound AZD2281 in women with recurrent ovarian cancer that is still responsive to platinum, whether their tumors have BRCA mutations or not.

In breast cancer, a similar opportunity may exist to treat an aggressive and stubborn class of tumors known as triple negatives. These cancers lack three clinical cancer markers, estrogen receptors, progesterone receptors, and the growth-promoting protein HER2. Because of this, the cells do not respond to anti-estrogen therapy, or to the HER2-targeted therapy trastuzumab.

Dan Silver, MD, PhD, then a research fellow with David Livingston, MD, found that triple negative breast cancers share features of BRCA-mutated tumors, including defects in DNA repair and an accompanying sensitivity to the DNA-damaging drug cisplatin. Could this parallel extend to sensitivity to PARP inhibitors?

Dr. Silver, now an assistant professor in the Women's Cancers Program, believes so. He has found that some of the tumors are very sensitive to PARP inhibitors when grown in the lab. This work is being translated in a clinical trial in collaboration with Judy Garber, MD, MPH, the director of the Friends of Dana-Farber Cancer Risk and Prevention Clinic. Building on the program's recent success using cisplatin chemotherapy to treat triple-negative breast cancers, the researchers plan to combine a PARP inhibitor with cisplatin, and treat women with newly diagnosed triple-negative tumors, with or without BRCA mutations.

Hitting the target

Alan D’Andrea, MD, has spent the last 15 years uncovering the genes and proteins involved in all six DNA repair pathways, and he thinks there may be more tumors with the right profile for PARP inhibitor treatment.

“Any cell that has become dependent on the PARP pathway for survival is fair game,” says Dr. D’Andrea, the chief of the Division of Radiation and Cancer Biology.

To sort out the cancers that qualify, Dr. D’Andrea and colleagues are working out a series of laboratory tests to determine, in tumor samples, which DNA repair pathways are active. Having that information up front will allow doctors to figure out which patients are the best candidates for PARP inhibitor treatment. “This is a really good opportunity for personalized medicine,” Dr. D’Andrea says. “Our challenge is to find the perfect patients for the PARP inhibitors.”

Many questions remain about the new approach. Which PARP inhibitors of several in the pipeline will emerge as the best? Should the inhibitors be combined with chemotherapy? Should they be used early in treatment, or later? Resistance to PARP inhibitors can emerge when cells find a way to reactivate the BRCA-dependent repair pathway – will that limit their use?

It will take time to get the answers, but Dr. Matulonis sees PARP inhibitors as just the beginning of a whole new class of therapies. “As time goes on we are going to see more and more drugs targeting DNA repair,” she says. “For women with ovarian cancer who don’t have the BRCA mutation, this is going to be an area of new drug therapies and active research. This is an exciting time.”

Women's Cancers Program physician/scientists Ursula Matulonis, MD, (left) and Dan Silver, MD, PhD, see promise in the use of PARP inhibitors for some breast and ovarian cancer patients.
By her side: Facing cancer together

Mary Kenn sits at home in Bridgewater, Mass., surrounded by familiar comforts. Framed photos of her three grown children and their families hang on her wall; the scent of fresh home-baked blueberry muffins fills the air; and, most reassuring of all, her companion of the last 44 years, her husband, Jim, is at her side.

There’s a soothing harmony between the Kenns, one in which their sentences and stories blend into one voice, even when they’re describing Mary’s three bouts with women’s cancers. “I get very involved,” Jim says, using the word “we” when talking about his wife’s treatments.

Mary Kenn became a patient at Dana-Farber/Brigham and Women’s Cancer Center (DF/BWCC) in spring 2008, when she was diagnosed with a rare cancer of the uterus and chose an experimental treatment. But her saga with women’s cancers goes back to 1997, when she underwent a lumpectomy for breast cancer; a year later she learned she had a different type in her other breast. “The second cancer required the whole works – mastectomy, chemotherapy, and radiation,” recalls Kenn, who received her care at a local hospital. “Each time something came up we’d say, ‘we’ll get this fixed,’” adds Jim.

Mary enjoyed good health while taking several medications to help prevent a recurrence. Nearly 10 years later, however, she noticed some mild vaginal bleeding. Her local gynecologist recommended a hysterectomy, and the lab report after that procedure showed carcinosarcoma of the uterus, an unusual type of cancer that grows in the muscle and lining of the uterus.

A second surgery was scheduled to fully stage the cancer, and although biopsies showed no sign of cancer beyond the uterus, Kenn elected to enroll in a clinical trial to give herself the best chances that the cancer would not return. “I thought this would be like an insurance policy,” she explains. “It would also help doctors find treatments for other women.”

The trial is testing a combination of radiation therapy with the chemotherapy drugs oxaliplatin and gemcitabine, a protocol used for other aggressive cancers, says Kenn’s Dana-Farber oncologist Susana Campos, MD, MPH. “We shared with the Kenns what we knew, and what we didn’t know about this very rare type of uterine cancer,” explains Dr. Campos. “For example, we do know there is a high risk of spread to the abdomen. But because the cancer is uncommon, there really is no standard of care, so an experimental approach made sense.”

Kenn, 65, finished treatment in December 2008 and returns for scans and check-ups. She and her husband sing the praises of DF/BWCC and especially their devoted nurse, Christin Whalen, RN. “I was nervous coming into Boston, and Christin put me at ease,” Kenn recalls. “She hugged us when we arrived, and often called us at home to see how I was.”

Today, the Kenns relish their roles as “Mima” and “Bampa” for their five grandchildren. Oldest daughter Alicia and her own daughter, Amanda, 22, live with them, and their other two children and families are nearby. A college student studying to be a nurse, Amanda says, “I love my Mima and Bampa more than oxygen.”

Thanks to her renewed health, Kenn can continue with one of her favorite hobbies: embroidering blankets and other gifts. After buying a computerized sewing machine she attended an embroidery class. As usual, her husband, Jim, was at her side.
Toward the end of her fourth pregnancy, Karen Puopolo, MD, PhD, realized something was not normal with her left breast. There was a lump, but Puopolo figured it was a blocked duct or something else related to her pregnancy. Both her breast-feeding consultant and OB/GYN assured her not to worry, and Puopolo — herself a physician and researcher — opted to “wait and see.”

But when her daughter Elizabeth Chloe was about nine months old and Puopolo began to wean her off breast feeding, the lump became more prominent. Puopolo, who specializes in newborn medicine at Brigham and Women’s Hospital, booked an evaluation at her hospital’s Comprehensive Breast Health Center. The ultrasound, mammogram, and two biopsies that followed revealed she had stage IIA invasive ductal carcinoma, a cancer that arises from cells lining the milk ducts. The disease had not spread to her lymph nodes.

At age 42, with four children and a full-time career, Puopolo was shocked, afraid, and mad. “I thought, ‘Oh, lord, I have an infant.’ I knew I had a small chance of having breast cancer, but I wasn’t expecting it,” she recalled recently in her Longwood Avenue office. “My husband told me I had to stay around and help him raise our children.”

Puopolo’s experience with a delayed diagnosis is not unique. Breast cancer is the most common cancer in pregnant and postpartum women, affecting roughly one in 3,000 pregnant women, according to the National Cancer Institute. The natural breast
fullness and tenderness during this life stage can interfere with early detection and diagnosis of these cancers.

Once her disease was found, Puopolo had four months of chemotherapy at Dana-Farber, taking doxorubicin (Adriamycin), cyclophosphamide (Cytoxan), and paclitaxel (Taxol) every two weeks. A mastectomy and reconstructive surgery followed, along with some additional anticancer medicines. The chemotherapy caused debilitating fatigue, nausea, and weight loss, but Puopolo's cancer responded well to the drugs.

This winter, Puopolo got discouraging news that she had a new nodule suspicious for breast cancer in her chest wall. A biopsy and then surgery to remove it revealed invasive ductal carcinoma. Although this cancer had not spread, a genetic test called Oncotype DX suggested that it had a higher-than-normal risk of recurrence. Puopolo's doctors recommended radiation therapy and six more months of chemotherapy. In addition, she opted for surgery to remove her ovaries and plans to take an aromatase inhibitor to help reduce the chance of recurrence through estrogen suppression.

She's also doing her best to stay in shape and remain healthy by routinely using the stairs and taking long walks around her Newton, Mass., neighborhood with her husband, Steve Melly.

Those strolls, along with support from her husband and kids — now ages 3 to 16 — have helped her through the ordeal, along with several other factors. Among them are her caregivers at Dana-Farber/Brigham and Women's Cancer Center. "Dana-Farber is a wonderful place," Puopolo says. "Everyone is kind, respectful, and professional. My oncologist Ann Partridge and her nurse practitioner Anne Kelly are great, and my oncology nurse Deb DiPrete is a godsend. I have the same medical team as before, and it now includes Dr. Jay Harris of Radiation Oncology."

Being a physician and researcher (she runs a small lab that investigates neonatal infectious diseases) has also made it easier to sort through the scientific literature and weigh various options for treatment. "I'm a very informed consumer," Puopolo says. "I want to believe everything is going to be fine, but I can't fool myself about my medical situation. However, I had a 100-percent risk of death if I didn't get treated."

Facing her fears has also helped Puopolo as a patient, physician, and mom. At a professional conference in Washington, D.C., last summer, she crossed paths with other women in academic medicine who were there to review their skills and career goals. During the three-day event, Puopolo realized that her breast cancer had kept her from crafting a five-year academic plan. She thought to herself, "I'm done being afraid. I can't stand around ignoring my life."

Puopolo urges women who are pregnant or breast feeding to pay attention to their bodies, despite the hormonal and other changes they're experiencing. "If something just doesn't seem right after a few months," she advises, "have it checked out." Good advice from a doctor who's been there.

"Dana-Farber is a wonderful place," Puopolo says. "Everyone is kind, respectful, and professional. My oncologist Ann Partridge and her nurse practitioner Anne Kelly are great, and my oncology nurse Deb DiPrete is a godsend."
Making a Difference

The National Cancer Institute estimates that in 2008 more than a quarter million women will have been diagnosed with breast or gynecological cancers; just shy of 69,000 will lose their lives to these diseases. Thanks to the vision and generosity of donors like you, Dana-Farber continues to offer women diagnosed with cancer the best in care while pursuing research that will lead to more effective and less toxic treatments. Our scientists continue to make progress on many fronts in their ongoing battle against these complex diseases. There are many ways in which patients, families, and friends can contribute as well.

Supporting the Research

Donated blood can help not only existing patients, but also research efforts at Dana-Farber. For information on how to donate blood, contact Brigham and Women’s Hospital Blood Donor Center at 617-732-6620. To donate platelets, contact the Kraft Family Blood Donor Center at 617-632-3206. Learn more online at www.dana-farber.org/how/donateblood.

To learn more about becoming a potential stem cell donor, call the National Marrow Donor Program’s Donor Recruitment office at 617-632-2561 or 866-875-3324.

Donating Funds

Through the generous support of donors, the Women’s Cancers Program has raised more than $62 million over the last 10 years, and nearly $11 million in fiscal 2008 alone.

To learn more about how you can support the battle against women’s cancers, call Ginny Fuller at 617-582-8832.