

SUSAN F. SMITH
CENTER FOR
WOMEN'S CANCERS



TURNINGPOINT

2019



Personalized Treatment for Women's Cancers

Matching therapies with each
unique patient

**Research Takes Aim
at Endometrial Cancer**

**Providing a Lifeline
to Patients in Need**

**How Pathology Unlocks
Cancer Cell Secrets**

TURNINGPOINT 2019

Alan D'Andrea, MD

Director, Susan F. Smith Center for Women's Cancers
Director, Center for DNA Damage and Repair

Sara M. Tolaney, MD, MPH

Associate Director, Susan F. Smith Center for Women's Cancers
Director, Clinical Trials, Breast Oncology

Eric P. Winer, MD

Chief Clinical Strategy Officer, Dana-Farber
Senior Vice President, Medical Affairs
Chief, Division of Breast Oncology

Ursula Matulonis, MD

Chief, Division of Gynecologic Oncology

Tari King, MD, FACS

Chief of Breast Surgery, Breast Oncology Program

Ross Berkowitz, MD

Director, Gynecology and Gynecologic Oncology
Dana-Farber Cancer Institute and Brigham and Women's Hospital

Jennifer Bellon, MD

Director, Breast Radiation Oncology
Dana-Farber Cancer Institute and Brigham and Women's Hospital

Judy Garber, MD, MPH

Director, Center for Cancer Genetics and Prevention
Dana-Farber Cancer Institute

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Dana-Farber shares patient stories which may include descriptions of actual medical results. Dana-Farber provides personalized care for each patient based on their unique needs; their experiences and results will vary.



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TURNING POINT
Dana-Farber Cancer Institute
Department of Communications
450 Brookline Ave., OS300
Boston, MA 02215
or call 617-632-4090
or email TurningPoint@dfci.harvard.edu

Editors: Michael Buller, Naomi Funkhouser

Art Director: John DiGianni

Managing Editor: Eric Schuller

Design: Lee Whale

Contributors: Nicole Davis, Austin Fontanella, Robert Levy, Kristin Baird Rattini, Megan Riesz, Richard Saltus, Riley Simmons, Saul Wisnia

Production: Aaron Lazauski

Photography: Sam Ogden



Alan D'Andrea, MD, director, and Sara Tolaney, MD, MPH, associate director, Susan F. Smith Center for Women's Cancers

A Message from the Directors

The value of cancer treatment is measured in lives saved, lives extended, and families kept whole. By that criteria, we've made extraordinary progress: For many types of cancer, the prospects facing patients today are substantially better than they were even in the recent past.

Scientists, too, evaluate their work based on its impact – on patients, certainly, but also on fellow researchers. A discovery or observation that captures the imagination of other scientists can be the impetus for an entirely new field of inquiry, and a springboard for research that ultimately garners National Institutes of Health funding. Unfortunately, funding opportunities for small-scale studies with the potential to greatly improve treatment are in short supply.

That's why we at the Susan F. Smith Center for Women's Cancers have invited teams of Dana-Farber scientists to compete for pilot grants to support new and promising research projects in breast and gynecologic cancers. We've created a

committee, headed by Dr. Sara Tolaney, that will solicit project proposals from investigators across the Institute and review them to identify the most promising ones. The committee will have representatives from a wide array of areas – basic science, clinical development, survivorship, outcomes research, patient advocacy, and others. The size of the grants will be modest, but as a spark for research ideas that otherwise might go unexplored, their impact can be substantial.

The need for such a program is clear. Despite improvements in cancer survival, much work remains to be done, particularly in areas such as overcoming drug resistance, deterring or halting metastasis, and preventing cancers from recurring. The key to accomplishing this is to personalize care for each patient – taking into account her medical history, the type and subtype of her tumor, the genomic particulars of her cancer and her immune system, as well as her stage of life, her lifestyle, her values and priorities. Each patient is a complex

mix of biology and personhood; treatments must respect and reflect that.

In launching the pilot grant program, we're counting on one of the Susan F. Smith Center's – and Dana-Farber's – greatest strengths: the diversity of scientific and clinical expertise of our faculty and staff. Together, they're often able to follow up on new discoveries in ways that researchers at few other institutions can. The result, in many cases, is a new avenue of research and a new approach to treatment.

One of the major effects of research into breast and gynecologic cancers, at all levels, is that we're increasingly able to tailor treatment to the specific nature of each cancer and each patient. This issue of *Turning Point* focuses on the trend toward personalization of treatment for women's cancers and how it's improving both survival rates and quality of life for many patients. We're proud of the leading role Dana-Farber scientists and clinicians are taking in this trend and look forward to sharing their progress with you.

UPDATES

At the Susan F. Smith Center for Women's Cancers, cancer care, clinical research, and basic research are parts of an ongoing cycle. Research into the basic workings of cancer cells and their interactions with the rest of the body provides leads for the development of new therapies. Clinical testing explores whether such therapies are safe and effective enough to become standard care for patients. And clinical care generates information and hypotheses that can be taken back to the laboratory to devise even better treatments.

Here is a brief look at how this dynamic is guiding our work.

Division of Breast Oncology



Eric P. Winer, MD

Researchers and clinicians in the Susan F. Smith Center for Women's Cancer are tackling some of the biggest challenges in breast cancer treatment – how to improve options for patients with triple-negative, inflammatory, and metastatic breast cancer – while developing new combinations of drugs, including immunotherapies, that can potentially benefit all patients.

In the area of triple-negative breast cancer, investigators are collecting tumor tissue samples to learn whether the tumor cells show genomic changes over time – information that may indicate which patients are likely to respond to therapy. In inflammatory

breast cancer, researchers are creating a tissue bank that includes hundreds of tumor samples to be used in a wide range of research projects and are leading trials of new, multidrug treatment regimens. The EMBRACE (Ending Metastatic Breast Cancer for Everyone) program, meanwhile, is streamlining care and fostering research for patients with metastatic breast cancer, reaching more than 2,500 patients so far.

Clinical trials are underway for several new approaches to breast cancer treatment. These include studies to determine how best to use drugs known as CDK4/6 inhibitors for patients with hormone receptor-positive breast cancer. Others are testing the effectiveness of immunotherapy drugs in combination with chemotherapy and other agents in various breast cancer types. And new programs such as B-PREP are working on strategies for preventing breast cancers from occurring or recurring.

Division of Gynecologic Cancers



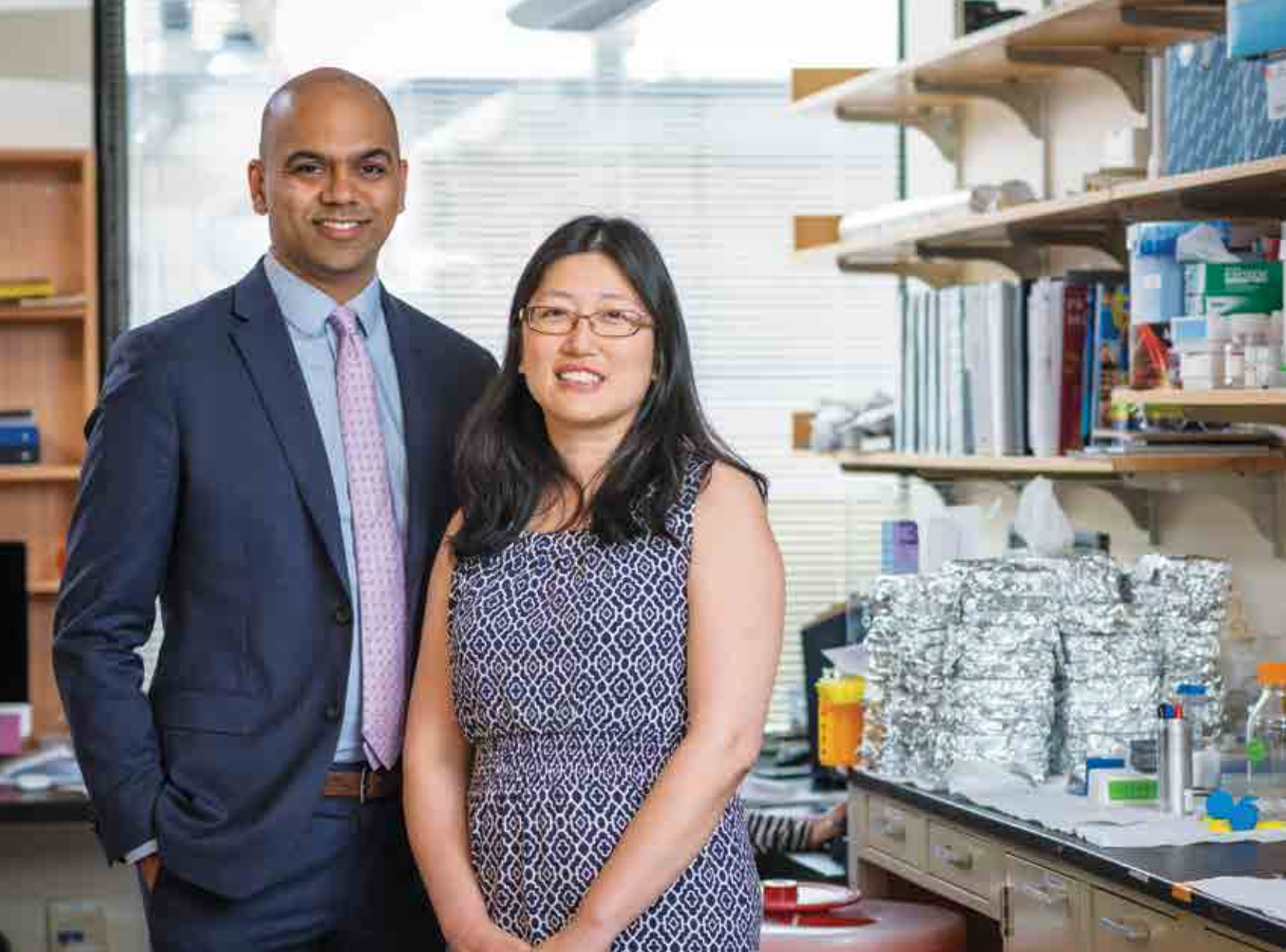
Ursula Matulonis, MD

From developing tests to predict who is most likely to benefit from particular therapies, to devising tests for detecting cancer at an earlier stage, to finding ways to overcome resistance to chemotherapy, to testing new combinations of drugs, including immunotherapy agents, our scientists are making progress against gynecologic cancers on multiple fronts.

In the area of early detection, for example, researchers have developed a test for detecting ovarian cancer in blood samples. Using microRNAs, molecules that help control gene activity, the test proved highly sensitive in initial studies, and

researchers are now exploring whether it can be used to identify ovarian cancer cells early in the course of the disease.

To overcome the problem of resistance, in which tumors don't respond or stop responding to specific drugs, researchers are analyzing tumor samples before and after therapy to determine whether they harbor differences that enable some cancer cells to evade chemotherapy. For patients who don't benefit from existing drugs, our investigators are working with Dana-Farber chemical biologists to design novel compounds and test prototypes in the labora-



Nikhil Wagle, MD, and Nancy Lin, MD, both lead research in metastatic breast cancer.

tory. One such agent would target a key part of the process by which cells use information stored in DNA.

A particularly promising area of clinical research involves combinations of immunotherapies and other drugs. In ovarian cancer, investigators are leading an array of clinical trials pairing immunotherapy agents with drugs that block blood growth, interfere with cancer cells' ability to repair their DNA, and deliver chemotherapy directly to tumor cells.

Center for Cancer Genetics and Prevention



Judy Garber, MD, MPH

The risk of developing breast or ovarian cancer varies widely, often due to genetic or other biological factors. A woman may have an increased risk because of an inherited disposition to these cancers, a family history of them, or exposure to certain environmental hazards. Specialists at our Center for Cancer Genetics and Prevention can help patients and their families understand their risk and map out ways to minimize it.

Research is a significant part of the center's work. One project involves screening Jewish women of Eastern European heritage, who have a higher-than-average rate of *BRCA* gene mutations linked to breast and ovarian cancer, to see if they carry these anomalies. The goal is to explore new avenues for encouraging at-risk populations to make use of genetic testing and counseling services.

A second, pilot study, is exploring whether a particular drug can benefit women with a *BRCA* mutation who are planning to have surgery to remove their ovaries and fallopian tubes in order to reduce their risk of ovarian cancer.

Ask an Expert

by Austin Fontanella

Will Radiation Oncology Help Change the Future of Cancer Care?

Radiation therapy has long played a vital role in cancer care. Today, as this therapy becomes more precise, the department of Radiation Oncology at Dana-Farber/Brigham and Women's Cancer Center (DF/BWCC) is using targeted radiation therapy to improve outcomes for more patients.

Pinpoint Accuracy

For patients diagnosed with certain gynecologic cancers, radiation therapy is mapped out by the millimeter. Using a procedure known as brachytherapy, temporary or even permanent radioactive sources are inserted directly inside a patient's tumor. Once radiation therapy is complete, the applicator is removed, and no radioactive sources are left within the body.

What makes brachytherapy ideal for treating gynecologic tumors is that highly radioactive sources can be placed directly within cervical or recurrent endometrial tumors for a precise period of time.

"One great thing about brachytherapy is that highly focused radiation can be delivered directly to the tumor in a manner that is not possible with external beam approaches," explains Martin King, MD, PhD, director, brachytherapy clinical operations.

While treating by the millimeter may sound precise, the technology is still improving. CT scans, which can overestimate the size of tumors, are being replaced by magnetic resonance imaging (MRI) simulators. And, at DF/BWCC, there are ongoing clinical trials aimed at tracking inserted applicators in real time, resulting in shorter procedure times and improved implants.

Larissa Lee, MD, director of gynecologic radiation oncology at DF/BWCC, is leading one such trial. By inserting a tracking device into one of applicators themselves, Dr. Lee hopes to skip multiple trips to the MRI room, and instead use live guidance to track the various brachytherapy needles.

"We're always looking for ways to make this process more efficient," Dr. Lee says. "By improving procedures, we're able to help more patients and be less invasive."

Dr. Lee adds, the plan isn't to stop there either. Instead, she hopes to one day be able to see real-time data when administering radiation. This would help radiation oncologists, like herself, identify "warm" and "cold spots" immediately, and adjust the applicators, or doses, accordingly.



Larissa Lee, MD

"In the future, we hope to more precisely deliver brachytherapy by using MRIs, as well as taking into account the biology of an individual patient's tumor," explains Dr. Lee.

Finding the Right Partnership for All Cancers

As Drs. King and Lee focus on identifying a more precise target, Jonathan Schoenfeld, MD, MPH, director of melanoma radiation oncology at DF/BWCC, is combining radiation therapy with immunotherapy. By doing so, he hopes to improve outcomes for more patients with all types of cancers.

"Think of radiation like taking an antibiotic to help fight an infection," says Dr. Schoenfeld. "By using radiation therapy, we may put our immune system in a better position to kill the cancer cells."

The idea behind the one-two punch is simple; when immunotherapy works, it's often effective for a long time. However, most people don't currently respond to this treatment. Meanwhile, while radiation has a high response rate, it doesn't always keep the cancer from coming back. By pairing the two treatments, doctors hope to find a combination that can take advantage of the strengths of both. While there are still questions to address, including whether combination therapy can help patients whose tumors don't respond to immunotherapy, Dr. Schoenfeld believes we are moving in the right direction.

"Radiation was once thought to inhibit the immune system, and now we're exploring if it can help stimulate it," he says.

New Clinical Trials Open for Endometrial Cancer Patients

Advances in the scientific understanding of endometrial cancer have helped spark a research revival into the disease, with four clinical trials led by Dana-Farber investigators enrolling patients in 2019. The trials are especially welcome for the 10-15% of patients with endometrial cancer who are diagnosed with an advanced stage of the disease. These patients almost invariably relapse after receiving standard therapy, at which point the disease generally can't be cured with existing drugs.

“Approximately 42,000 women in the U.S. are diagnosed with endometrial cancer each year,” says Panos Konstantinopoulos, MD, PhD, director of translational research in gynecologic oncology at the Susan F. Smith Center for Women's Cancers. “For the 90% of patients with early stage disease, standard therapy is curative. For patients with later-stage disease, we urgently need novel treatments.”

Dana-Farber research into the biology of endometrial cancer suggests promising new ways of attacking the disease with targeted therapies as well as immunotherapies. Dr. Konstantinopoulos and his fellow scientists approached several pharmaceutical firms with proposals for clinical trials involving their drugs. Their initiative resulted in four phase II trials:

- A trial led by Dr. Konstantinopoulos combines an immune checkpoint inhibitor called avelumab and a PARP inhibitor called talazoparib. Checkpoint inhibitors clear the way for an immune system attack on cancer; PARP inhibitors undermine cancer cells by impeding their ability to repair damaged DNA. The trial will explore whether pairing avelumab with a PARP inhibitor is effective in patients with “microsatellite stable” (MSS) endometrial cancer.
- A trial led by Jennifer Veneris, MD, PhD, of gynecologic oncology combines the checkpoint inhibitor pembrolizumab with an antibody-drug conjugate called mirvetuximab. Pembrolizumab targets an immune checkpoint protein called PD-1; mirvetuximab joins an antibody to a drug molecule that targets a key structure in fast-dividing cancer cells. The trial is open to patients with MSS endometrial cancer whose tumor cells have a folate receptor α on their surface.
- A trial led by Dr. Konstantinopoulos combines the targeted drug abemaciclib, a new drug compound called LY3023414, and hormonal therapy in patients with high-risk endometrial cancer. (LY3023414 targets a cancer cell enzyme called PI 3-kinase; abemaciclib interferes with a key phase of the cell cycle.) Between 70 and 90% of endometrial cancers are fueled by the hormone estrogen and initially respond to hormone-blocking therapy, but eventually relapse. Investigators hope to overcome the problem of drug resistance by adding abemaciclib and LY3023414, which strike two parts of the same molecular pathway, to hormone-blocking therapy.
- A trial led by Joyce Liu, MD, MPH, director of clinical research in gynecologic oncology, focuses on the targeted therapy AZD1775 in patients with high-grade serous uterine cancer, which accounts for 10-15% of endometrial cancers. Such cancers are aggressive and usually recur after standard therapy.

Each trial addresses a shortcoming of standard therapy or a problem identified in previous trials of novel drugs, Dr. Konstantinopoulos says. Collectively, the four trials will enroll between 150 and 200 women. Investigators hope to complete the trials in the next two years. Learn more at www.dana-farber.org/clinicaltrials.

Gynecologic Cancer Research and Clinical Trials

Researchers in the Susan F. Smith Center's Division of Gynecologic Oncology explore gynecologic cancers from a wide variety of scientific angles – from discoveries about the genes that cause tumors to develop and grow, to investigations of immunotherapies, to studies of ways drugs can be combined to fight recurrent cancer. Find a complete list of our latest clinical trials online at www.dana-farber.org/clinicaltrials.



\$20 Million Gift for Metastatic Breast Cancer Research

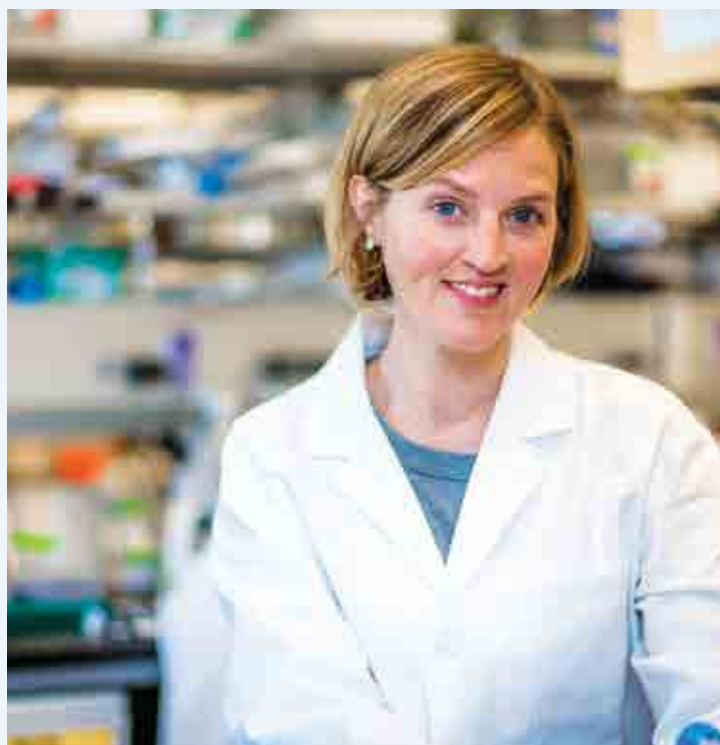
A \$20 million gift announced in June 2019 from the Saverin Family will establish the Saverin Breast Cancer Research Fund at Dana-Farber Cancer Institute under the direction of Eric P. Winer, MD, senior vice president for Medical Affairs for Dana-Farber, chief of the Division of Breast Oncology in the Susan F. Smith Center for Women's Cancers, and the Thompson Chair in Breast Cancer Research at Dana-Farber. This transformational gift provides powerful momentum toward the Institute's comprehensive campaign, currently in the quiet phase.

The Saverin Family's commitment is the largest individual gift for breast cancer research in Dana-Farber's history and their first major gift to Dana-Farber. The sole purpose of the Saverin Family's gift is to support research relating to treatment and eventual cures of advanced or stage IV metastatic breast cancer. Metastatic breast cancer is cancer that has spread outside of the breast and to other parts of the body, such as the bones, brain, liver, or lungs. It is a treatable but currently an incurable form of breast cancer.

A world-renowned leader in the breast cancer field, Dr. Winer has made seminal contributions to improve the treatment of this disease, with a focus on the aspects of

breast cancer that remain the most challenging.

"The Saverin Family's foresight will allow us to tackle the unsolved challenges by building on the advances we have already forged, and to develop entirely new strategies," said Dr. Winer. "Their exceptional generosity provides resources we need to further metastatic breast cancer research that is underway, and, more importantly, to open bold avenues of investigation."



Heather Parsons, MD, MPH, is one of many faculty members who conduct research in metastatic breast cancer.

The Saverin Breast Cancer Research Fund will help to advance studies focused on resistance to hormonal treatments and targeted therapies. Advisory boards with experts from Dana-Farber and external organizations will help to steer research supported by the Saverin Breast Cancer Research Fund to achieve true advances over the next five years.

"This gift will make a profound difference in the lives of people living with breast cancer today and in the future, and we are incredibly grateful to the Saverin Family," said Laurie H. Glimcher, MD, president and CEO, Dana-Farber Cancer Institute. "Their

visionary investment will make our outstanding breast cancer program that much stronger in reaching key discoveries for patients worldwide."



The Metastatic Breast Cancer Project

Metastatic breast cancer patients across the country are joining the metastatic breast cancer project to help advance research and treatment. Learn more by visiting www.mbcproject.org or following @MBC_Project on Twitter.

Clinical Trial Underscores Promise of Immunotherapy for Ovarian Cancer

A combination of an immunotherapy drug and a DNA repair-blocking agent can be significantly more effective than either drug alone in women with hard-to-treat ovarian cancer, a phase I/II clinical trial led by Dana-Farber researchers indicates. The trial, known as TOPACIO/Keynote-162, offers compelling evidence that immunotherapies, which rarely have an impact against ovarian cancer as single agents, can produce a powerful anti-cancer response in tandem with other drugs. A report on the trial is published this year in *JAMA Oncology*.

The trial tested a combination of pembrolizumab – which targets the checkpoint protein PD-1 on immune system T cells – and the PARP inhibitor niraparib – which interferes with cancer cells’ ability to repair damaged DNA – in 62 patients with ovarian cancer that was resistant to platinum chemotherapy. The investigators found that the drug pair produced complete or partial responses – total or limited shrinkage of ovarian tumors – in 18%

of patients. Sixty-five percent of participants had their disease kept under control, including three patients with complete responses, eight with partial responses, and 28 with stable disease. That compares to response rates of less than 5% in similar patients treated with PARP inhibitors alone, and 9% in patients with ovarian cancer treated with pembrolizumab alone.

The results are especially impressive given that study participants had received multiple earlier treatments for ovarian cancer, and therefore represented an especially hard-to-treat group, trial leaders say. Some participants had undergone up to five previous treatments, and more than half had already been treated with bevacizumab, a drug that closes off cancers’ access to the bloodstream.

“These results are extremely promising for this set of patients, who have had several previous treatments and don’t respond to platinum chemotherapy, and therefore have few other treatment options available,” said Dana-Farber’s

Panagiotis Konstantinopoulos, MD, PhD, the lead author of the study. “Some participants are continuing to benefit from the therapy more than 18 months after starting it.”

The combination of niraparib with pembrolizumab in the trial follows laboratory research by Dana-Farber scientists, suggesting that PARP inhibitors and immunotherapy would make a synergistic pair, Dr. Konstantinopoulos says. PARP inhibitors allow cancer cells to accumulate DNA damage, which makes the cells more visible – and vulnerable – to the immune system. The results of the new trial set the stage for further studies of combinations of PARP inhibitors and immune checkpoint inhibitors in ovarian cancer as well as other solid cancers.

The study was supported in part by a Stand Up to Cancer-Ovarian Cancer Research Fund Alliance-National Ovarian Cancer Coalition Dream Team Translational Research Grant, which is led by Dr. Alan D’Andrea.



PARP inhibitor study leaders included (left to right) Panagiotis Konstantinopoulos, MD, PhD; Ursula Matulonis, MD; Jean Zhao, PhD; Liya Ding; Qiwei Wang; and Hye-Jung Kim, PhD.

Study Identifies *BRCA* Patients Who May Benefit from PARP Inhibitors

It may not be sporting to hit someone when they're down, but when the foe is a cancer cell, there's no merit in mercy.

That's the principle behind drugs known as PARP inhibitors. Tumor cells that lack effective *BRCA* genes have difficulty repairing certain kinds of DNA damage, potentially leaving them vulnerable to agents that inflict more DNA damage or further impede the repair process. PARP inhibitors do the latter. In tumors where *BRCA* genes are missing or mutated, combinations of PARP inhibitors and other drugs have produced impressive results in many patients.

However, the benefits aren't universal, and even when remissions do occur, they tend to not be lasting. Patients with high-grade serous ovarian cancer (HGSOC), for example, who have inherited mutations in the *BRCA1* or *BRCA2* gene often respond well to PARP inhibitors. Within five years, however, the vast majority of them relapse.

In a recent study, researchers led by Dana-Farber's Dipanjan Chowdhury, PhD, and Yizhou He, PhD, uncovered a major genetic contributor to this type of drug resistance.

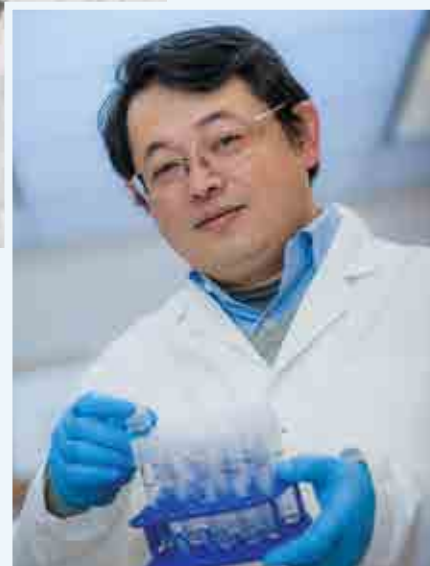
Using HGSOC cells with defective *BRCA1*, the investigators shut down 17,000 genes, one at a time, to determine which were responsible for resistance to PARP inhibitors. This comprehensive approach allowed them to generate a catalogue of genes whose loss may cause resistance to PARP inhibitors in *BRCA1*-deficient tumors. Of the several genes identified, the most notable was one that generates a protein called DYNLL1.

The discovery, reported in the journal *Nature*, may help doctors determine which patients with HGSOC deficient in *BRCA1* are likely to be resistant to PARP inhibitors: those whose tumor cells are without functional DYNLL1 probably wouldn't respond to the drugs and might benefit from other treatments.

"Our findings may also lead to new treatment strategies for these types of ovarian tumors," Dr. Chowdhury says. "Now that we know that loss of DYNLL1 has a role in PARP inhibitor resistance, we can investigate whether the loss of this protein creates new vulnerabilities in cancer cells. This may inspire the development of drug combinations that don't produce PARP inhibitor resistance."



Dipanjan Chowdhury, PhD



Yizhou He, PhD

The researchers also explored why the loss of DYNLL1 blunts the effectiveness of PARP inhibitors in HGSOC tumors with *BRCA1* mutations.

BRCA1 makes repairs when both strands of the DNA molecule have been broken. Before repairs can begin, one of the loose ends from each strand must be trimmed back so the strands can reconnect properly. The researchers found that DYNLL1 stands in the way of this end-snipping. In cells where DYNLL1 is lost, therefore, DNA repair can get underway. And that, in turn, enables the cells to brush off the effects of PARP inhibitors – to become PARP inhibitor-resistant.

"Our next step will be to explore ways to overcome such resistance," says Dr. He. "We're creating a library of cells with all the genes known to contribute to resistance and will use it to test drug combinations that may counteract resistance. Although *BRCA1* mutations are usually thought of in connection to breast and ovarian cancer, they can play a role in a wide variety of cancers. The need for resistance-proof drug combinations is high."

PARP Inhibitors Rouse Immune System Against Some Ovarian Cancers, Says New Study

Drugs known as PARP inhibitors have transformed treatment of some ovarian and breast cancers by sabotaging tumor cells' ability to keep their DNA in working order. But, in a recent study published in the journal *Cell Reports*, Dana-Farber scientists found that PARP inhibitors may also endanger tumor cells on a second front – by sparking an immune system attack on them.

The discovery, made in animal models of a common type of ovarian cancer, not only reveals PARP inhibitors to be a double threat to cancer cells, but suggests that combining PARP inhibitors with an immunotherapy agent can extend remissions triggered by the drugs.

“Three PARP inhibitors have been FDA-approved for the treatment of ovarian cancer with mutations in the *BRCA* genes. These represent the first targeted therapies approved for ovarian cancer, the number one cause of gynecologic cancer-related death,” said senior author Jean Zhao, PhD, of the Susan F. Smith Center. “The effectiveness of PARP inhibitors in these cancers has been thought to be due entirely to the direct killing of tumor cells. We show that the immune response provoked by the drugs plays a key role in cancer cell death as well.”

PARP inhibitors work by hindering cells' ability to repair

breaks in single strands of their DNA. In cancer cells that are already having difficulty fixing two-stranded breaks – because of a mutation or other abnormality in the *BRCA1* or *BRCA2* genes – the loss of single-strand repair can be a lethal blow. As DNA damage accumulates, the tumor cells gradually become dysfunctional and destroy themselves for the good of the body.

Dr. Zhao and her colleagues found that when tumors deficient in *BRCA1* are treated with PARP inhibitors, the tumor cells increase their output of PD-L1 – an “immune checkpoint” protein that renders them invisible to the immune system. Drugs known as checkpoint inhibitors are capable of removing the immune system's blinders so an attack on the tumor can proceed. The researchers found that mice treated with combination of the PARP inhibitor olaparib and an immune checkpoint inhibitor lived longer than those treated with olaparib alone.

“This observation has important implications for the treatment of ovarian cancer,” said Ursula Matulonis, MD, chief of Gynecologic Oncology in the Susan F. Smith Center and a co-corresponding author of the study. “When combined with other agents such as PD-1 inhibitors, PARP inhibitors can have enhanced anti-cancer activity, and we now know why.”



Jean Zhao, PhD

Susan F. Smith Center Faculty Recognized as 2019 ASCO Leaders in Care

Judy Garber, MD, MPH, and Ann Partridge, MD, MPH, both from the Susan F. Smith Center for Women's Cancer at Dana-Farber, were recognized in May 2019 by the American Society of Clinical Oncology (ASCO) with the society's highest honors. Recipients of these awards have worked to transform cancer care around the world.



Dr. Garber was awarded the ASCO-American Cancer Society Award and Lecture, which honors distinguished lecturers who have made a significant contribution to cancer prevention and control research or practice. Dr. Garber is the Susan F. Smith Chair and chief of the Division of Cancer Genetics and Prevention at Dana-Farber and a profes-

sor of medicine at Harvard Medical School. She conducts research in clinical cancer genetics, with a focus on breast cancer genetics. She is a leader in research on treatment and prevention of inherited breast and other inherited cancers, and an expert on Li-Fraumeni Syndrome. Her translational research focuses on the evaluation of novel agents targeting DNA repair defects in breast cancer.



Dr. Partridge was recognized with the Ellen L. Stovall Award and Lecture for Advancement of Cancer Survivorship Care, which is given to an extraordinary individual who has made multiple, significant, and enduring contributions to cancer survivorship care. Dr. Partridge is a professor of medicine at Harvard Medical School, and vice chair of medical

oncology at Dana-Farber, where she serves as director of the Adult Survivorship Program and leads the Smith Center's Program for Young Women with Breast Cancer. She and her team have characterized a range of issues of young breast cancer survivors, including the impact of treatment on fertility, adherence with hormonal therapy, psychological adaptation to the diagnosis including impact of treatment on sexual functioning, and the factors that play an important role in patient decision-making.

Dana-Farber Scientists and Associates Receive Major Grant from Gray Foundation

Scientists at Dana-Farber, the University of Texas, and the University of Pennsylvania in 2019 received a four-year, \$3.75 million Team Science Grant from the Gray Foundation to study the cascade of changes that occurs within cells when a key mechanism for repairing damaged DNA breaks down. The grant, announced following a national competition, is one of the first to be awarded by the Gray Foundation's Basser Initiative, which fosters research in cancers linked to mutations or malfunctions in the *BRCA* gene pathways.

BRCA genes work in concert with other genes to edit out and correct spelling errors in the DNA code. In people who inherit or develop mutations in *BRCA1* or *BRCA2*, the genes no longer perform this function as well, resulting in an accumulation of DNA damage that can cause normal cells to turn cancerous. Men and women who carry mutated forms of these genes have a significantly elevated risk of developing breast, ovarian, pancreatic, and/or prostate cancers.

The mission of the Basser Initiative Team Science Grant Program is to fund highly meritorious research projects that bring together the best minds in cancer research to develop new therapies, prevention approaches, and better understanding of the fundamental mechanisms at work in *BRCA*-related cancers. Funded projects are multidisciplinary and, preferably, multi-institutional.

Innovation Fund Grants Announced at Executive Council Breakfast

The 16th annual Susan F. Smith Center for Women's Cancers Executive Council Breakfast held in April 2019 attracted more than 300 women business and community leaders, and it raised more than \$250,000 for research at Dana-Farber. The annual breakfast presents the latest cutting-edge research and treatment being conducted at Dana-Farber to help eradicate women's cancers. Funds raised support the Smith Center's Innovation Fund for new research.

The event, which is also an opportunity for Susan F. Smith Center investigators to talk with attendees about their work

and answer questions in an informal atmosphere, featured discussions of prevention and early-detection strategies for breast and gynecologic cancers set the stage for a patient's perspective on the choices that cancer-risk tests can present.

Alan D'Andrea, MD, director of the Susan F. Smith Center gave an update on the center and announced the 2019 Susan F. Smith Center for Women's Cancer Innovation Fund grant recipients. The grants are for up to \$75,000 each and are given for basic, clinical, translational, or population science research projects related to breast and/or gynecologic malignancies.



Alan D. D'Andrea, MD, director of the Susan F. Smith Center for Women's Cancers

The 2019 recipients are:

- **Rinath Jeselsohn, MD**, breast oncology physician. Project title: Exploiting the Clonal Dynamics during the Acquisition of Resistance to CDK4/6 Inhibition in WT and Mutant ER for Novel Therapeutic Strategies in Estrogen Receptor Positive Breast Cancer
- **Jennifer Ligibel, MD**, director, Leonard P. Zakim Center for Integrative Therapies and Healthy Living. Project title: Body Mass Index and Breast Cancer Gene Expression in Women with Early-Stage Breast Cancer
- **Beth Mittendorf, MD, PhD**, director Surgical Research, and director, Breast Immuno-Oncology Program. Project title: Characterization of the Immune Microenvironment in Triple Negative Breast Cancer: Correlative Studies for the TOPACIO Trial Evaluating the Combination of PARP Inhibition and PD-1 Blockade
- **Huma Rana, MD**, clinical director, Center for Cancer Genetics and Prevention. Project title: Optimizing Treatment-Focused Genetic Testing in Metastatic Breast and Ovarian Cancer Patients

The leaders of the project, titled "Dissection of *BRCA*-mediated Tumor Suppression Pathways," include Alan D'Andrea, MD, Dipanjan Chowdhury, PhD, Panos Konstantinopoulos, MD, PhD, of Dana-Farber's Susan F. Smith Center; along with Patrick Sung, PhD, of the University of Texas Health Science Center; and Roger Greenberg, MD, PhD, of the University of Pennsylvania Epigenetics Institute.

"Our Team Science Project will provide valuable information about how inactivation of *BRCA1* or *BRCA2*, the activation of *BRCA*-independent DNA repair, and the acquisition of secondary mutations in regulators of *BRCA*-dependent DNA repair leads to cancer," says Dr. Chowdhury. "The work will help women who have inherited a *BRCA* mutation from their parents or whose *BRCA1* or *BRCA2* gene has been altered because of DNA damage. The knowledge garnered from our endeavors will endow medical practitioners with the wherewithal to counsel women regarding cancer risk, to predict the durability of drug efficacy, and to explain how drug resistance arises. Importantly, the results from our project will provide the foundation for the development of improved cancer treatment regimens."



Panos Konstantinopoulos, MD, PhD

Four years ago, Elizabeth McCabe discovered she was among an unlucky minority of patients with endometrial cancer. After her initial diagnosis, McCabe underwent surgery to remove her uterus and hoped that would be the end of her cancer journey. But a couple of months later, her doctors in her hometown, discovered what her body already knew: Her cancer had metastasized to her liver and lymph nodes. Her tumors had blossomed in silence, sprouting from the lining of the uterus and spreading to other parts of her body.

On the Cusp of a Sea Change in ENDOMETRIAL CANCER

Researchers are finding new, more targeted ways to thwart the most aggressive forms of the disease

By Nicole Davis

Endometrial cancers like McCabe's are challenging to treat because they have breached the confines of the uterus, so standard therapies are often largely ineffective.

"The good news is that the vast majority of patients with endometrial cancer are diagnosed early and cured," explains Panos Konstantinopoulos, MD, PhD, director of translational research in gynecologic oncology at Dana-Farber's Susan F. Smith for Women's Cancers. "But about 10-15% of patients have tumors that are extraordinarily difficult to treat. And for those patients, we don't have enough options beyond the standard regimens."

After three different courses of chemotherapy, McCabe's cancer remained undeterred. "I was basically told to get my affairs in order," she recalled.

She did. She and her family also researched what more could be done, which led her to Dana-Farber. She met with Dr. Konstantinopoulos, who had recently launched a phase 2 clinical trial in endometrial cancer – one of a handful now underway at Dana-Farber focused on finding potent new therapies for advanced forms of endometrial cancer.

Expanding Immunotherapy's Reach

Today, one of the most promising areas of clinical investigation in endometrial cancer is immunotherapy, a relatively new approach that stokes the fires of a patient's own immune system – energizing it so it can help quash tumor growth. Immune checkpoint inhibitors, a form of immunotherapy, have yielded profound results in some cancers. Yet initial tests in endometrial cancer were less dramatic: Only a small percentage of patients responded. That left researchers wondering: How can endometrial tumors be made more vulnerable to immune checkpoint inhibitors?

In an earlier clinical trial, Dr. Konstantinopoulos and his colleagues found that the immune checkpoint inhibitor avelumab was highly effective when given to a subset of endometrial cancer patients whose tumors showed a high propensity for accumulating genetic mutations. For patients with this molecular feature, known as microsatellite instability (MSI), avelumab would likely be a treatment option.

In endometrial cancer, only about 30% of patients have MSI; the rest have microsatellite stable (MSS) disease. Nevertheless, MSI has become an important biomarker of endometrial tumors, and it has begun to open the door to new treatments for patients, including McCabe,

with advanced endometrial cancer.

Shortly after her first visit to Dana-Farber, McCabe learned that her cancer exhibited MSI and she enrolled in a new clinical trial led by Dr. Konstantinopoulos. The trial involves a control group, where patients with MSI receive the immune checkpoint inhibitor avelumab and another group, comprising MSS patients, receive avelumab combined with a second drug, talazoparib (a PARP inhibitor that hinders cancer cells by interfering with their DNA repair). Dr. Konstantinopoulos and his colleagues hope that by combining these two drugs, they can make MSS tumors more susceptible to the effects of checkpoint inhibitors.

For McCabe, treatment with avelumab has been transformative. "Liz has had an extraordinary response," says Dr. Konstantinopoulos. "Her tumors began to shrink after just the first cycle of treatment."

McCabe says she feels like she has part of her old life back. "I got to see my daughters graduate from college and begin their first professional jobs," she said. "I look at all the things I've been given and I'm forever grateful for this trial."

Meanwhile, other Dana-Farber trials are examining targeted ways of attacking endometrial cancer. For example, the Smith Center's Jennifer Veneris, MD, PhD, is studying pembrolizumab, a checkpoint inhibitor, combined with mirvetuximab, a so-called antibody-drug conjugate. "Antibody-drug conjugates are antibodies hooked up to a chemotherapy agent, and they work kind of like a smart bomb, delivering chemo directly to cells," says Dr. Veneris.

Because antibodies recognize and bind to proteins that sit at the cell surface, they can be used therapeutically to home in on specific cell types. Mirvetuximab is designed to latch on to tumor cells that have a protein on their surface that is abundant on endometrial cancer cells.

Another challenge MSS tumors pose is that they are considered immunologically "cold." That is, they fail to provoke a strong response by the immune system. Antibody-drug conjugates, however, are believed to also fire up the immune



Jennifer Veneris, MD, PhD

system, particularly within and around a tumor. "We like to think of this as a way to make a tumor immunologically 'hot,'" says Dr. Veneris.

By pairing the antibody-drug conjugate with a checkpoint inhibitor – a kind of one-two punch – Veneris and her colleagues hope to make MSS tumors more susceptible to immune-mediated attack.

Additional trials underway also seek to address shortcomings of other existing treatments – from overcoming resistance to hormone-blocking therapy to targeting a highly aggressive subtype of endometrial cancer.

"These trials are all investigator-initiated, representing years of effort," said Ursula Matulonis, MD, director of gynecologic oncology in the Smith Center. "All of the drug combinations are entirely new, so we're in discovery mode. This is a critical unmet need, so we feel we're making a difference."

Reining in Metastasis

In addition to exploring new drug combinations, researchers are also delving into a fundamental question: What enables endometrial tumors like McCabe's to spread in the first place?

Dana-Farber oncologist and researcher Rameen Beroukhim, MD, PhD, is leading a team of scientists probing the genomes of



Rameen Beroukhim, MD, PhD

hundreds of endometrial tumors, including primary tumors and their corresponding metastases. What they have uncovered so far seems a bit surprising: Within individual patients, the metastases appear more similar to each other than to the primary tumor – like a cluster of leaves budding from a tree branch.

“That makes us think that only a small focus of the tumor is actually spreading and that much of the rest of the tumor is unable to do so,” explains Dr. Beroukhim.

His team is carefully comparing the genomes of the metastases with those of their corresponding primary tumor, searching for a genetic “smoking gun.” That is, gene mutations that appear in the metastases but not in the primary tumor, which could explain how those parts of the tumor gained the wherewithal to spread. If the team can pinpoint genes that drive metastasis, they offer potential fodder for future drug development. Indeed, drugs that could prevent metastasis would represent a fundamental advance for many cancer types.

Building a Better Model

As Dr. Beroukhim and his colleagues plumb the depths of endometrial tumor genomes, Dana-Farber researchers are also working to improve how these cancers are studied in the lab. That means developing animal models that more closely mimic

the biology of human tumors.

Jean Zhao, PhD, leads a lab developing innovative models of gynecological cancers using meticulous genetic engineering approaches in mice. These models incorporate many of the same mutations and driver genes that fuel cancer in humans, often weaving together two or three mutations into the same tumor. In addition to common genetic origins, the tumors also share cellular and biological hallmarks of their human counterparts.

Importantly, Zhao's mice are immunologically intact, a crucial feature that enables researchers to carefully analyze the complex interplay between tumors and the immune system. “Once we have the right model for endometrial cancer, we can study it in a variety of ways, including with targeted therapies, immunotherapy, and even combinations of the two,” says Dr. Zhao.


Unintended Consequences

While a lack of good models has plagued endometrial cancer researchers for decades, clinicians have faced another vexing problem: the unintended consequences of the hormone-modulating drug tamoxifen. The drug is often given to women over the course of several years to help treat or prevent breast cancer. But, like many therapies, its actions are not wholly beneficial.

“We've known for many years that tamoxifen treatment can increase the risk of endometrial cancer,” said Rinath Jeselsohn, MD, an oncologist and researcher at Dana-Farber. “The overall risk is fairly low because endometrial cancer is not a common cancer, but tamoxifen can raise a patient's risk of the disease by anywhere from two- to six-fold.”

In the breast, tamoxifen suppresses cell growth. But in the uterus, it has the opposite effect, nudging cells toward a cancerous fate. Now, Dr. Jeselsohn is spearheading an effort to figure out just how tamoxifen goads uterine cells – specifically, what genes and biological processes it causes to run amok. She is scrutinizing the genomes of tumors from patients with tamoxifen-associated endometrial cancer, searching for genomic signals that distinguish the disease from other forms of endometrial cancer. Her goal: to find a way to molecularly disarm the effects of tamoxifen on the uterus, perhaps by designing drugs that can be given together with the hormone modulator.

As Dr. Jeselsohn looks forward to this possibility, McCabe also anticipates what lies ahead. Her cancer is still in retreat. Every two weeks, she flies to Boston for an infusion of avelumab. Her care team has become like a second family, so she does not mind the trip. Most of all, McCabe is excited for the future.

“Before, I'd hesitate if someone asked me to do something in six months or a year, but now I can make longer range plans,” she said. “It makes me feel very hopeful.” 

PERSONALIZED

matching therapies



TREATMENTS

by Robert Levy

with each unique patient, not just her disease

A rose is a rose, but cancer is a chameleon, often differing from one patient to the next, even in patients with cancer of the same organ or tissue.

At Dana-Farber's Susan F. Smith Center for Women's Cancers, doctors tailor treatments to the specific characteristics of each cancer and each patient. In addition to the traditional questions about a tumor's type, size, aggressiveness, and degree of metastasis, physicians are likely to focus on factors fundamental to the cancer's survival and growth. These include the bad actors within a tumor's genome, the proteins and immune system signalers on its surface, and its vulnerability to specific drug agents.

"Personalizing treatment makes it possible to match the strengths of a particular therapy to the weaknesses of a specific tumor," says Ursula Matulonis, MD, chief of Gynecologic Oncology at Dana-Farber and Brock-Wilson Family Chair. "Years of research and clinical experience have taught us which thera-

pies, in which combinations, work best in particular groups of patients with particular cancers, and we have much to learn as well. Our goal is to find customized treatments that put our knowledge to work for all of our patients." This approach can in some cases improve quality of life by ensuring that patients don't receive more treatment than necessary, or treatments that are unlikely to be effective.

Susan F. Smith Center physicians also are customizing treatment in ways that go beyond strictly medical considerations and address patients' personal values and priorities. A woman's family or career goals, her concerns about the long-term side effects of certain treatments, her stage of life – all may be considered in the treatment approach she and her physician choose.

An Abundance of Considerations

In breast cancer, a wide range of factors come into play when crafting a treatment plan, says Sara Tolaney, MD, MPH, director of the breast oncology clinical trials program and associate director of the Susan F. Smith Center. The first is whether the disease is metastatic or confined to the breast. Tumor samples are then analyzed to determine whether the cancer cells carry receptors for the hormones estrogen and progesterone, and whether they test positive for the HER2 protein.

“At initial diagnosis, we determine which of these three subtypes of breast cancer the patient has: hormone receptor-positive, HER2-positive, or triple-negative,” Dr. Tolaney says. “We also assess whether the patient has other health conditions that influence the optimal treatment regimen.”

Personalizing therapy involves making finer and finer distinctions within each subtype of cancer. Often, that involves molecular tests to determine whether the tumor cells harbor specific genetic abnormalities or carry certain telltale proteins on their surface. Many patients with metastatic breast cancer, for example, have their tumor tissue molecularly tested in Dana-Farber and Brigham and Women’s Hospital’s Profile program for genetic irregularities.

For breast tumors that have not metastasized, physicians follow a similar process of zeroing in on the appropriate treatment. In some cases, this involves examining how well a tumor responded to a previous therapy. This is particularly clear in the case of “neoadjuvant” treatment, in which patients receive drug therapy to shrink their tumor prior to surgical removal.

“In patients with stage 2 or 3 HER2-positive tumors, recent data show that patients who received Herceptin [a drug targeting such tumors] plus chemotherapy before surgery, but

still had breast cancer cells in the tissue removed at the time of surgery, did much better if they then switched to the drug T-DM1, compared to those who just continued Herceptin,” relates Nancy Lin, MD, associate chief of the Division of Breast Oncology at the Susan F. Smith Center. T-DM1 consists of a chemotherapy agent tethered to Herceptin: the Herceptin acts like a courier delivering the chemotherapy directly to the tumor. “We learned that we can improve outcomes by tailoring the treatment based on response to pre-operative therapy.”

For all the impact that molecular research is having on cancer treatment, physicians also take a variety of more familiar, “macro” factors into account. Among these is a patient’s age. Susan F. Smith Center physician-researcher Rachel Freedman, MD, MPH, for instance, is leading several clinical trials exploring whether reduced-toxicity therapies can still produce good results for older patients with breast cancer while decreasing side effects.

Ann Partridge, MD, MPH, founder and director of the Susan F. Smith Center’s Program for Young Women with Breast Cancer, describes how other, more personal considerations can factor into treatment. “For younger women who desire to have children after their breast cancer therapy, we offer referral to our fertility specialists to see if embryo or egg preservation should be considered prior to chemotherapy. There are also some chemotherapy regimens that we can choose to use for patients that may have less impact on fertility and medicines that can be given concurrently with chemotherapy to try to preserve fertility.”

Is Less More?

Personalized treatment often involves more narrowly targeted therapies, but it need not mean more therapy in total. A

Here are some examples of how the treatment decision-making process works for metastatic breast cancer:

- Triple-negative tumors are tested for the presence of PD-L1, a protein that protects the cancer from an immune system attack. Patients whose tumors test positive for PD-L1 may be treated with chemotherapy and an immunotherapy drug that blocks PD-L1 and exposes the tumor to an immune system assault.
- Patients are also recommended to undergo genetic testing to see if they have a *BRCA* gene mutation. If the test comes back positive, patients are often treated with drugs known as PARP inhibitors, which undermine cancer cells’ ability to keep their DNA intact.
- Patients whose tumors are found to carry the estrogen receptor are treated with drugs known as CDK4/6 inhibitors, which work by stalling the process of cell division. If the tumor has a mutation in the PI3K gene and stops responding to a CDK4/6 inhibitor, research suggests it can be controlled by a combination of hormonal therapy and a drug called alpelisib, which blocks PI3K. Alpelisib was recently approved by the Food and Drug Administration, but there are many questions about how it should be used in clinical practice, particularly because it has a number of side effects.

major focus of recent research by Eric Winer, MD, in fact, is whether “less can be more” in the treatment of some breast cancers.

Dr. Winer, chief of the Division of Breast Oncology at Dana-Farber, is quick to point out that a “less is more” approach is suitable only for specific subsets of patients. He cites two areas where the approach has worked “phenomenally well.”

The first involves women with breast cancer that is hormone receptor-positive and HER2-negative, which has a relatively low risk of recurring, and is highly sensitive to hormone-blocking drugs. Standard treatment calls for hormonal therapy in combination with a substantial course of chemotherapy, but “over the past five years we’ve learned that these patients can still do very well if we pull back on the amount of chemotherapy,” Dr. Winer remarks. The second example involves women with early-stage, HER2-positive breast cancer, who are commonly treated with chemotherapy and the HER2-targeting drug Herceptin. Here, too, clinical trials have shown that patients can be safely and effectively treated with very limited amounts of chemotherapy.

Both examples stem from a desire to ease the sometimes painful and draining side effects of chemotherapy without reducing the effectiveness of treatment. “All of our therapies have the potential to cause side effects, which can in some cases have profound consequences for patients,” comments Joyce Liu, MD, MPH, director of gynecologic oncology clinical research at the Susan F. Smith Center. “Even in situations where 90% of patients tolerate a treatment well, 10% are still having complications. If we can use our understanding of the differences between tumors to cut down the use of unneeded treatment and reduce that suffering – in a way that’s safe – we need to try.”

Customizing Gynecologic Treatments

The treatment of gynecologic cancers is personalized in many of the same ways as breast cancer treatment – with a focus on cancer type, genomics, and the patient’s age, health, and life goals.

Panos Konstantinopoulos, MD, PhD, director of translational research in Gynecologic Oncology, illustrates how cancer



Panos Konstantinopoulos, MD, PhD



Nancy Lin, MD

subtype influences treatment in ovarian cancer. “The most common histological subtype is high-grade serous ovarian cancer, but there are others, like clear cell, low-grade serous, low-grade endometrioid, and mucinous ovarian cancers,” he explains. “They all have their own molecular underpinnings, and we treat patients differently. For some subtypes, like low-grade serous, for example, we use hormonal therapy more frequently. Other subtypes, like mucinous ovarian cancers, are treated more like gastrointestinal tumors.”

And, as in breast cancers, treatment is often tuned to tumors’ genomic susceptibilities. Ovarian cancers hampered from repairing their DNA are often treated with PARP inhibitors or ATR/Chk1 inhibitors, which put the brakes on cancer cell division. In endometrial cancer, as in breast cancer, physicians want to know if the cells sport hormone receptors on their surface and if they have a DNA-repair deficiency. So, too, in cervical cancer, where the presence of PD-L1 on the tumor cell surface prompts treatment with the drug pembrolizumab.

“Genetic research has allowed us to understand that each tumor is different and to look for the genetic alterations that are driving tumors,” Dr. Konstantinopoulos remarks. “This work, in combination with clinical research, has helped us understand why certain drug agents work well for some cancers and not others, why some patients develop resistance to certain drugs and others don’t, and how to find novel drugs for these patients. As this work advances, so will the use of personalized therapy.” ^{TP}

PROVIDING

A hand reaches out from the right side of the frame, palm facing forward, against a bright, hazy sky at sunset. The sun is low on the horizon, creating a lens flare and casting a warm glow. In the foreground, there is a field of tall, green grass. In the background, there are rolling hills or mountains under the same sky.

On a cool spring day, a patient we'll call Claudia arrived at Dana-Farber's Susan F. Smith Center for Women's Cancers for blood tests and chemo, but there was more on her mind than the weather.

Her biweekly appointments, while essential to her care, were wreaking havoc on her life. She had recently been forced to leave her job; it offered no sick days or vacation time. Facing the same restrictions at work, and serving as her primary caregiver, her husband had to quit, too, and the double loss of income led to an eviction notice. The couple couldn't afford an apartment near the school their two children attended, and the waiting list for subsidized housing was months long.

As she followed the clinic assistant to get her vital signs checked, Claudia wondered what the future held for her and

her family.

There are many challenges patients must face in addition to – or resulting from – their breast or gynecological cancer. Whether it is financial constraints, relationship issues, language barriers, or concerns over how to navigate the dating world after diagnosis, the center's experienced Social Work staff is there to help ensure that all parts of a patient's well-being are considered. No matter their age, background, or type of cancer, women can find the help they need to maintain a satisfying life.



A LIFELINE

WHEN CANCER AFFECTS QUALITY OF LIFE, HELP IS AVAILABLE

by Saul Wisnia

Different Women, Different Needs

“The burden of cancer is felt differently by each woman,” says Nancy Borstelmann, PhD, MPH, senior director of social work at Dana-Farber. “For instance, our clinical work and research shows us that younger women, on average, have higher levels of stress, anxiety, and depression than someone older who has weathered more storms in his or her life or relationships. Some women are more open to talking about the impact of diagnosis, while others have barriers to their care that make reaching them more difficult. We want to be there for all of them, and for their caregivers too.”

Borstelmann, who has more than 20 years of experience at Dana-Farber, says that the growing body of research into issues faced by female patients has enabled clinicians to offer more specialized guidance and treatment. One example is the Young and Strong Program, in which women with breast cancer under age 45 receive comprehensive care, support, and education tailored to this age group: fertility concerns, questions

around school and careers, and the challenges of dating, intimacy, and raising children while living with cancer. Clinical social workers are a key part of the Young and Strong team, helping patients work through their concerns and sometimes complex emotions.

“Young single women may be worried about managing the dating world, and how and when they should talk about their illness with potential partners, at the same time they are adjusting to changes in their bodies,” says Julie Salinger, LICSW, a clinical social worker at Dana-Farber for nearly a decade. “During and after cancer treatment, issues with intimacy and sexuality are common. Early menopause may occur, causing symptoms which some patients are not comfortable discussing with their medical team. Many feel there is no solution. We make sure to ask patients about all of these issues, to normalize their experience, urge them to seek further help, and to provide valuable, helpful information that can alleviate symptoms.”

Those patients with children on their mind, explains Salinger, face a different set of concerns. “If women have children, we provide information about how best to talk to children of differing ages, even rehearsing future conversations with them,” Salinger says. “If they want to have children, or want to have more of them, we can help them explore the possibilities – and process grief if this is not possible.”

Barriers in Any Language

The well-meaning parents of 20- and 30-something cancer patients are a less obvious challenge. They are often more than ready to let their daughters move back home, or to care for grandchildren while mom is undergoing treatment. These acts of kindness, social workers have learned, can come with an emotional cost – a feeling of displacement or regression. Such emotions can also hamper older female patients whose adult children step in as their caregivers. After decades of driving, cooking, and taking care of things themselves, giving up these responsibilities can feel like a loss of independence.

Rachel Freedman, MD, MPH, a breast cancer specialist in the Susan F. Smith Center, has studied issues facing older patients. Thirty percent of breast cancer patients in the United States are now age 70 or older, and are more likely to

have other health conditions that can complicate their breast cancer treatment. They also are often dealing with a shrinking support network and logistics around getting to and from appointments, as well as financial considerations. As longer-term survivorship for ovarian cancer and other gynecological cancers increases, so too does the need to offer patients of all ages support for issues outside their direct care.

“We are deeply committed to not only improving the length of one’s life by treating their cancer, but we are also completely focused on the quality of life that women with cancer have,” says Dr. Freedman. “Whether it is side effects from treatment, both short- or long-term, better support, or emotional health, we are driven to make our treatments as tolerable as possible while providing as much benefit as we can.”

For some patients, language can also be a barrier. Clinical social worker Rachel Allende, LICSW, specializes in working with limited English-proficiency patients, of which Spanish speakers are the largest group. She collaborates closely with interpreters and encourages patients to join *Círculo de Vida*, a monthly support group for Dana-Farber’s Spanish-speaking patients. Its membership has become a source of support for one another.

No matter what language they speak, patients can face financial and related challenges that are further deterrents to care. With housing in the Boston area becoming increasingly expensive, Allende and other social workers are seeing more patients like Claudia who are forced to leave their jobs, go without meals, or even become homeless while dealing with cancer. Because people are not always forthcoming about such issues, especially if language is a barrier, Allende strives to ask the right questions.

“We all do our best to meet people where they are at, and as colleagues we are always seeking out each other for help depending on who may have the best resources,” says Allende. “Whether it is housing security, food security, legal issues, or people who need shelter, the key is knowing who to contact for a patient’s other concerns beyond cancer.”

Addressing these concerns is a fundamental intervention to help manage distress and support quality patient care. Traditionally, oncologists, nurse practitioners, and nurses have determined which patients they feel would best benefit from



Nancy Borstelmann,
PhD, MPH



Social workers at Dana-Farber Cancer Institute

a social work referral. But a new group is now also helping: patients themselves.

On their fourth medical oncology “encounter” – which usually occurs in their second or third visit – breast oncology patients are now asked to complete a brief survey known as the Illness Impact Questionnaire. This tool includes a measure of an individual’s level of anxiety and depression, which helps alert social workers as to which patients are experiencing higher levels of distress and may be most in need of counseling.

“We ask to what extent they are worried about the impact of their cancer on common areas of concern: their children, caregivers, spirituality, and their sexual functioning and emotional well-being,” says Borstelmann. “There are also questions about practical barriers to care, like transportation, and if they score at a level of moderate distress or concern, the results of the screening advance to the patient’s provider for review. In addition, a social worker will make a follow-up call.”

Social work referrals have risen since the distress scale screenings first started last year. The hope, says Borstelmann, is that even if their score does not warrant a referral, the act of answering the questionnaire may raise patients’ awareness of the help available, which may lead patients to seek help.


Another highly effective resource for helping patients connect with social work services involves individuals who have faced similar challenges. The Susan F. Smith Center offers the SoulMates program, which matches breast cancer patients with former patients who have been through a similar experience.

These peer mentors are trained in topics such as listening, problem-solving, and confidentiality. Through one-on-one conversations, they provide emotional support and help relieve fears. Speaking of her SoulMates mentor, one patient said, “I could share my deepest darkest thoughts and fears – and I knew that she would understand.”

A patient’s spouse, partner, parents, and children may also feel anxious, and social workers provide these and other caregivers with their own support as needed – along with helping to identify options for community- based support.

“We respect how difficult it is for caregivers of patients to make time to talk to someone when they are already dealing with so many responsibilities outside their normal life,” says Salinger. “For efficiency’s sake, we may assign a separate social worker to a partner and arrange an appointment to coincide with the patient’s treatment schedule.”

In the end, it is all about making a patient’s quality of life better. Working with Claudia, the patient who found herself evicted during treatment, Allende helped the family find space in a shelter with a semi-private room, critical for a woman who is immunocompromised. Then, over time, she helped them access an apartment and get their kids into a new school, all while providing emotional support to the entire family.

Claudia can now focus her attention to treating her cancer, knowing that as additional challenges arise, she has a team at the Susan F. Smith Center to help her – even when she is not within its walls. 



CO

Marisa R. Nucci, MD
Director
Women's & Perinatal Pathology

Marisa Nucci, MD



AXING SECRETS

FROM CANCER CELLS

by Robert Levy

Susan Lester, MD, PhD

As a pathologist-in-training in the early 1990s, Deborah Dillon, MD, remembers viewing a sample of lymphoma tissue under a microscope and thinking, “I know that every one of the tumor cells has a particular chromosomal abnormality, but I can’t see it.’ It was frustrating – would there ever be a way to peer into the genetic makeup of cells?”

Wish granted. DNA sequencing is extending the reach of pathology into regions of the cell that once seemed impossibly remote. A field once defined by what could be seen with the naked eye or under a microscope has embraced technology for probing specific genetic errors within tumor cells – to the point where molecular pathology is now a field unto itself. It's a mark of how far the field has advanced over the past 25 years that, today, Dr. Dillon – a specialist in breast cancer pathology at the Susan F. Smith Center for Women's Cancers – is herself a molecular pathologist.

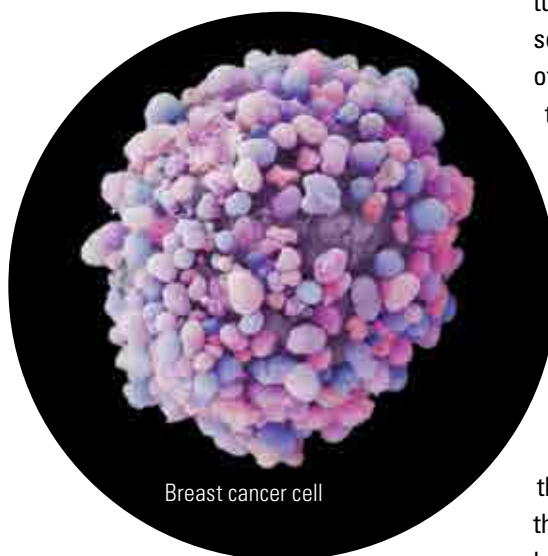
As the treatment of women's cancers becomes increasingly personalized – keyed to the specific characteristics of each patient and each patient's cancer – the field of pathology has more than kept pace. It might even be said that pathology invented personalized medicine: its concern with individual differences has become the model for cancer care as a whole.

Pathology's Part

At the most basic level, pathology is the branch of medicine concerned with diagnosing disease based on an examination of organs, tissues, and fluids from the body. In oncology, pathologists are the physicians who examine tissue to evaluate, first, if a patient has cancer or related disease and, if so, what type, whether and how far it has spread, how aggressive it is, and other information that will guide treatment. In women's cancers, for example, pathologists determine whether a breast tumor is hormone receptor-positive (meaning its growth is fueled by estrogen or progesterone), and whether ovarian cancer has metastasized or remains within the ovaries.

Pathologists describe their role as providing the starting point for therapy. "A pathology exam is fundamental to a patient's

care," says Susan Lester, MD, PhD, a breast cancer pathologist in the Susan F. Smith Center. "Treatment can't begin until a diagnosis is made. In breast cancer, for example, we're looking at slides to determine if the cancer is noninvasive or invasive and if it expresses hormone receptors or is positive for the HER2 protein. These are the major determinants of how a patient is treated."



Although pathologists are not clinicians, in that they usually don't see patients, they are very much part of the clinical team, working closely with oncologists and others directly involved in treatment. "The pathologic diagnosis is the hub around which the treatment of patients rotates," says breast pathologist Stuart Schnitt, MD, chief of breast oncologic pathology, Dana-Farber/Brigham and Women's Cancer Center. "If you don't have the right diagnosis, patients can't possibly receive the right treatment."

"If you know pathology, you will be a better physician" – My father, an orthopedic surgeon, told me this before I began clinical rotations as a medical student," says Marisa Nucci, MD, director of gynecologic

pathology at the Susan F. Smith Center. "What I came to realize is that pathology is at the core of care. To quote [Canadian physician] Sir William Osler, 'as is our pathology so is our practice.'"

Means of Interrogation

Pathologists' means for making a diagnosis are many and varied. Like a stubborn defendant on a witness stand, tumor cells do not always yield their secrets easily. Pathologists, in the role of cross-examiner, subject tumor tissue to a variety of tests to wrest as much information as they can from each specimen. They examine the tissue without the aid of a microscope to note its shape, size, color, and weight. They view it under a microscope to ascertain what the cancer cells look like, how they compare to normal cells (the closer the resemblance, the better the prognosis, in general), and whether they've spread to nearby tissue and lymph nodes. They use immunohistochemical studies on glass slides to identify specific proteins in cancer cells. They run cytogenetic tests to find chromosomal abnormalities. And, as part of the Profile program at Dana-Farber and Brigham and Women's Hospital, women with metastatic breast cancer and many patients with gynecologic cancers have the opportunity to have their tumor tissue analyzed for genetic abnormalities that may be susceptible to drugs being tested in clinical trials.

Molecular analysis of tumor tissue allows for more deeply informed decisions on treatment but can't replace traditional microscope-based techniques. "The approaches complement each other," Dr. Lester remarks. "They provide fundamentally different pieces of information; it's when you put them together that they

become very powerful.”

“For example, we now use special techniques such as immunohistochemistry to evaluate whether a tumor has a defect in mismatch repair and is more likely to respond to immunotherapy,” Dr. Nucci observes. “In addition, we are beginning to use molecular sequencing to help uncover targetable mutations for individualized treatment.”

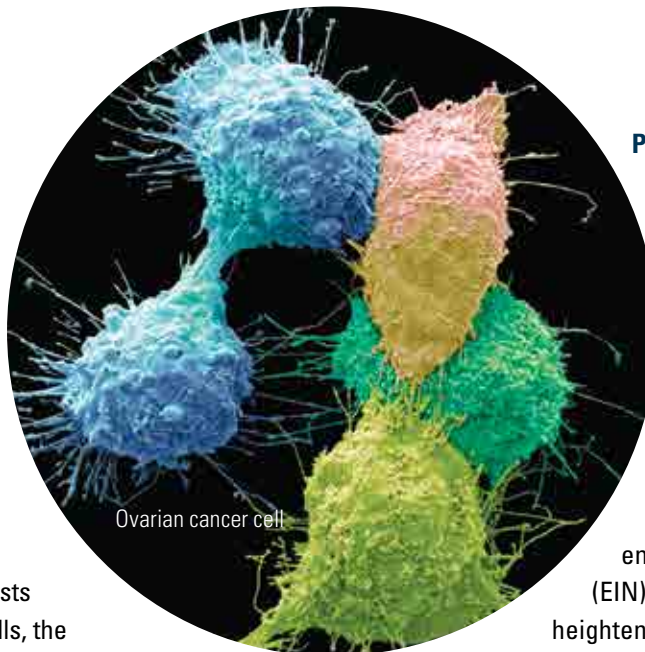
The more information pathologists can coax or coerce from tumor cells, the better they can pin down the precise nature of the cancer and treat it accordingly. “We now have the opportunity to refine our system for classifying tumors by factoring in molecular data,” Dr. Dillon says. “In the end, that should lead to better treatment.”

The Collaborative Approach

The classic image of a pathologist may be of a white-coated physician working alone at a microscope, but pathologists routinely collaborate with other pathologists and clinicians, particularly in difficult cases where a second – or third, or fourth – set of eyes can be helpful. “Subtleties within a tumor sample can make diagnosis challenging,” Dr. Schnitt states. “It can be a question of, ‘Is this breast cancer HER2-positive or not; is it really a grade 3 cancer; are there signs that blood or lymph vessels have been invaded by the tumor?’” Multi-headed microscopes that enable multiple pathologists to view a specimen simultaneously allow for a sharing of expertise. Difficult cases are also presented at tumor boards, periodic meetings at which pathologists and clinicians from several disciplines review and discuss diagnoses and treatment options of specific patients.

It is at these meetings, and in their daily interactions with physicians and other clinicians, that pathologists are most fully in their element. “I’m a gynecologic pathologist, but in many ways my intellectual orientation and the colleagues I work most closely with are clinicians,” says George Mutter,

MD. “We’re not here just to make diagnoses. We want to make patients’ lives better, and we do that by being part of a team that manages patient care.”



Ovarian cancer cell

Practice and Prevention

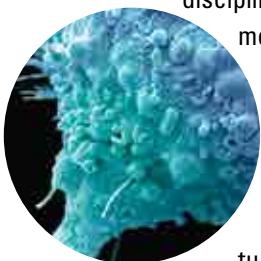
Making accurate diagnoses begins, but doesn’t exhaust, pathology’s place in personalized cancer medicine. Pathologists allied with the Susan F. Smith Center have, for example, made important advances in women’s cancers prevention. Dr. Mutter and his colleagues identified a condition known as endometrial intraepithelial neoplasia (EIN), which places women at greatly heightened risk of developing endometrial cancer. Patients with the condition can choose

to be closely monitored for signs of endometrial cancer or undergo a procedure to prevent the cancer from occurring. The discovery by gynecologic pathologist Christopher Crum, MD, that many ovarian cancers originate in the fallopian tubes may lead to new approaches for preventing this cancer as well.

Other Susan F. Smith Center pathologists are exploring whether genomic alterations in cancer cells track with changes in tumor behavior. Breast cancer pathologist Beth Harrison, MD, and her colleagues have collected tissue samples of rare breast cancers and are utilizing Oncopanel – the DNA-sequencing technology used in the Profile program – to identify genomic changes within them. “We’ve found some interesting molecular changes that suggest tumors with certain pathologic features may be more aggressive than we would have expected based on their traditional pathologic classification,” she explains.

In other research, Dr. Harrison, with Tari King, MD, chief of breast surgery at Dana-Farber/Brigham and Women’s Cancer Center, and breast surgeon Faina Nakhliis, MD, genomically profiled samples of high-grade lobular carcinoma in situ (LCIS) – areas of abnormal breast cell growth that significantly raise a woman’s risk of breast cancer. “We found highly prevalent alterations in the gene for HER2, which could serve as a molecular marker for this type of LCIS,” she relates. Although there currently is no clinical test for this alteration, the discovery raises the possibility of a new way to identify women with this condition.

These research efforts and others suggest that pathology’s future is as wide-open as the one Dr. Dillon imagined at the start of her career. **TP**





Jennifer Guerriero, PhD, works to understand why tumors may be resistant to immunotherapy, and identify novel targets for treatment.

Young Investigators Exploit Patient Samples for Cancer Studies

by Richard Saltus

In their search for better treatments for breast, ovarian, and other cancers, young investigators Jennifer Guerriero, PhD, and Sarah Hill, MD, PhD, rely on a precious commodity — patient tissue samples obtained by surgeons in the Susan F. Smith Center for Women’s Cancers.

Studies of these normal and cancerous tissues, which are collected, banked, and grown in the laboratory, are helping researchers understand why tumors are vulnerable to certain drugs and resist others. Examination of the microenvironment of the tumor cells (that is, the matrix of connective tissue and various types of cells interacting with the tumor cells) is shedding light on the role of immune cells surrounding the tumor; some of those cells can suppress an attack on the cancer, while others can fuel the attack.

“I have an amazing opportunity to work with world-renowned scientists and clinicians at Dana-Farber and to bridge the basic

and translational science we’re doing in the lab using clinical samples from patients who have undergone biopsies or surgical procedures,” says Dr. Guerriero.

Dr. Guerriero is director of the Breast Tumor Immunology Laboratory (B-TIL), which she has been building together with her mentor, Elizabeth Mittendorf, MD, PhD, the Rob and Karen Hale Distinguished Chair in Surgical Oncology and director of Dana-Farber’s Breast Immuno-Oncology Program.

The B-TIL lab obtains samples of blood, tumors, and other patient tissues for studies focused on the immune regulation of breast cancer. Making use of this precious tissue, Dr. Guerriero



Sarah Hill, MD, PhD, uses organoids to help identify effective treatments for ovarian cancer patients.

is working to understand why tumors may be resistant to T-cell immunotherapy, and to identify novel targets for immunotherapy. She is especially interested in the role of immune cells, and the relationship of T-cells and macrophages, cells, which can suppress the immune system's ability to fight tumors, but also can be part of an antitumor response.

Dr. Guerriero notes that women with breast and ovarian cancer may initially respond to therapy with PARP inhibitor drugs, but usually relapse because the cancer becomes resistant. There is evidence, she says, that suppressive macrophages surrounding the tumor eventually sap the power of the T cells to fight the tumor. However, with funding from the Susan G. Komen organization, Guerriero is studying the potential of eliminating suppressive macrophages from the tumor, or even "teaching those macrophages to become anti-tumor macrophages."

Sarah Hill, MD, PhD, is a women's and perinatal pathologist by training, and an associate pathologist in the laboratory of Alan D'Andrea, MD, director of the Susan F. Smith Center. A major focus of her research is ovarian cancer, and she has been using cancer cells from surgical specimens to create "organoids" — minuscule spheres of cells that mimic a tumor. She and D'Andrea are testing the potential of ovarian organoids

to rapidly screen drugs and identify those that are likely to be effective against a specific patient's tumor.

Dr. Hill is always excited to get a call from an operating room at Brigham and Women's Hospital when a new patient tumor sample is available. She carries a bag containing wet and dry ice and special vials to hold the specimens as she dashes several blocks from the operating room to the D'Andrea laboratory, where the cancer cells are processed and grown in laboratory culture. On weekends she does the painstaking work of dividing the tumor cells and placing them in laboratory dishes with the nutrients they need to thrive and grow.

The organoids that develop from the patients' cells take a few days to a week to form. They are very small, "but if you hold the plate up to the light, you can see the dots" that are the organoids, and functional capabilities of each patient's unique tumor can be deciphered in a matter of days to weeks.

Ovarian cancer is particularly interesting to her because some of the tumors have a defective DNA damage repair mechanism that can be exploited by drugs like PARP inhibitors and newer DNA damage agents. Dr. Hill's work now focuses on understanding the mechanisms of specific DNA damage repair defects in ovarian cancer and how best to target them with funding from the Department of Defense Ovarian Cancer Research Program and the American Association for Cancer Research.

Dr. Hill says she knew she wanted to be involved in science and medicine from a young age, in part because of medical issues — one of which required an MRI scan of her brain when she was in third grade: she found it all fascinating. After graduating from Harvard, she spent a year at Oxford University as a Rhodes Scholar, studying yeast genetics. Returning to Boston, she earned her medical degree at Harvard Medical School and her PhD at Harvard University, in the laboratory of David Livingston, MD, chair of Dana-Farber's Executive Committee for Research.

Immunotherapy Helps Patient Live Well with Endometrial Cancer



Laura Dickerman and her husband, Myron, have been fortunate enough to see the pyramids of Egypt, the classic cars that line Cuba's streets, the famous art museums in Russia, and other well-known sights around the world.

Today, Dickerman's travels are closer to home: She commutes from Sharon, Massachusetts, to Dana-Farber's Susan F. Smith Center for Women's Cancers every two weeks for immunotherapy. But the travel time into Boston has been worth it: Dickerman's cancer has shown no evidence of growth in the past two years – and doctors say her case is an example of how endometrial cancer treatment has greatly improved recently.

"There have been some very promising results from trials of immunotherapy, by itself or in combination with other targeted agents," says Joyce F. Liu, MD, MPH, director of clinical research in the Division of Gynecologic Oncology in the Susan F. Smith Center. "I think this trial has really allowed Laura to have a quality of life she might not otherwise have had."

In 2014, the day after Christmas, Dickerman woke up in the middle of the night and noticed she had abnormal vaginal discharge. She went to the hospital, where she was referred to her gynecologist for further examination. After a biopsy, she was

diagnosed with endometrial cancer.

She had a hysterectomy, but in late 2015, Dickerman developed a severe cough. A chest X-ray revealed that the cancer had spread to her lungs. Dickerman was referred to Liu, and she started with standard chemotherapy. However, her cancer grew through one regimen of chemotherapy, and on the second, she had side effects requiring a dose reduction.

At just that time, Dr. Liu and her colleagues in the Division of Gynecologic Oncology were starting to investigate whether immunotherapy could treat endometrial cancer. Since chemotherapy had not proven to be a very good option for Dickerman, Dr. Liu enrolled her in a clinical trial that was testing single-agent avelumab – an immune checkpoint inhibitor – in recurrent or metastatic endometrial cancer. Dickerman's tumor initially shrunk by 60%, and it hasn't grown since.

Today, Dickerman comes to Dana-Farber for her infusion with Myron by her side. She is experiencing some side effects from the checkpoint inhibitor, including a rash, neuropathy, and worsened arthritis – but the side effects of chemotherapy would have been much more significant, according to Dr. Liu.

"Our understanding of uterine cancer has evolved significantly from where it was even five years ago, and we now understand that, like other cancers, there are different types of uterine cancer, each of which will likely have its own set of specific vulnerabilities

Immunotherapy Success in Hard-to-Treat Breast Cancer

First diagnosed in late 2013, Rita McGuire O'Brien's triple-negative inflammatory breast cancer recurred soon after extensive treatment including chemotherapy, a mastectomy, and radiation. The disease continued to progress despite chemotherapy.

O'Brien, who lives in Fall River, Mass., says that after the cancer recurred, she felt "depressed and not hopeful." Then, while being treated at Dana-Farber, she met Sara Tolaney, MD, MPH, breast oncologist and associate director of the Susan F. Smith Center for Women's Cancers.

Dr. Tolaney told her about a new clinical trial for patients like her. The phase 1 study was testing a combination of immunotherapy and chemotherapy for triple-negative breast cancer. The rationale was that immunotherapy – which hadn't yet shown effectiveness in breast cancer – might be spurred to greater potency by the addition of chemotherapy.

O'Brien began the combination trial in April 2015 and is still

in treatment. She comes to Dana-Farber once a week for three weeks, receiving nab-paclitaxel (chemotherapy) and atezolizumab, the immunotherapy antibody, and takes one week off.

Today, the only remnant of her cancer is a small lymph node in her armpit that shows on scans, "and it's not clear if this has active cancer in it or not at this time," says Dr. Tolaney.

"I'm very grateful, and will never again give up hope," says O'Brien. In December, it will be five years since her initial diagnosis – a very good outcome for patients with triple-negative breast cancer.

It's important to note that O'Brien responded better than most who participated in the phase 1 trial. But even in the group of patients with recurrent breast cancer, 39 percent of patients responded and the median survival rate was nearly 15 months.

Learn more in the longer version of this article at <http://blog.dana-farber.org/insight>.

Speech Language Pathologist Draws Inspiration from Her Patients



As a speech pathologist for cancer patients at Dana-Farber, Maria Puglia is no stranger to cancer's emotional toll. But after discovering a lump in her left breast in February 2018, she was about to experience cancer from the patient's perspective.

After Puglia's tumor was biopsied, she learned she had HER-2 positive breast cancer. HER-2 is a growth-promoting protein on the outside of breast cells; if the cells produce too much HER-2, it can lead to cancer.

As a mother of three children and a health care professional, Puglia took a practical approach and wasn't uncomfortable asking tough questions.

"I flat-out asked my doctor, 'Do you think I'll live long enough to get my [9-year-old son] to college,'" she recalls. "And he looked at me and said, 'I think that we can make you a grandmother. What do you think about that?'"

That positive prognosis was encouraging during Puglia's treatment. With the help of her oncologist Harold Burstein, MD, PhD, Puglia underwent a mastectomy of her left breast and six rounds of a TCHP chemotherapy regimen. During treatment, Puglia used a scalp cooling cap. The cap chilled her head, narrowing the blood vessels beneath the skin while she received chemotherapy. As a result, less chemotherapy reached her hair follicles, decreasing hair loss.

Puglia drew from her experience as a speech language pathologist to navigate her life during and after cancer.

"I knew that a majority of people can have a fulfilling life with cancer and post-cancer," says Puglia. "I would always tell people that I got more out of my patients than they got out of me. I took all the vignettes, all the stories of people that I found so brave and inspiring and I remember thinking to myself, 'If this ever happens to me, I want to be like them.'"

Puglia remembered the stories and remained strong after treatment. She had to stay on the H (herceptin) and P (perjeta) drugs for months after finishing her TCHP treatments, and she completed her final round of HP in April 2019. In the future, she hopes to establish a charity that can make scalp cooling caps more accessible to cancer patients.

that we can target," Dr. Liu says. "I am definitely optimistic about our future advances in this disease."

Although their trips abroad are no longer possible, Dickerman still takes short trips around the area to see extended family and friends. Her children and grandchildren all live in Sharon or close by.

"I have been so lucky to be a patient at Dana-Farber, and I cannot say enough about my team," Dickerman says. "The help, cheerfulness, and care I have received is remarkable. Every person I have come in contact with has made me feel like I was their most important patient and has given me their undivided attention. I hope that the results of the trial I'm on will turn out to be lucky for other women as well."

Ovarian Cancer Survivor Sings a Song of Hope



It was a bumpy road for Anne Sandstrom at first: After dealing with a stage IIIc ovarian cancer diagnosis, she had two relapses in three years. But finally, treatment worked, and Sandstrom has enjoyed 16 years in remission — enough for her oncologist Ursula Matulonis, MD, chief of Gynecologic Oncology in the Susan F. Smith Center, to declare her "graduated" in 2017. The 62-year-old musician and author no longer needs to come in for checkups.

So why is Sandstrom continuing to talk about her journey, after her doctor gave her the all-clear? As Sandstrom sees it, by spreading the word about her experience with late-stage ovarian cancer, she aims to provide hope to other patients.

"When my doctor told me, 'you're free; you don't have to come here anymore,' I started to cry," says Sandstrom. "But I never considered stopping doing everything I could to help my doctor and everybody else learn as much as they can from me."

While ovarian cancer remains difficult to treat, especially in its later stages, treatment options for the disease have rapidly expanded. Researchers now have a much better understanding of the molecular forces at work in ovarian cancer than they did before, owed in large part to clinical trials, Dr. Matulonis says.

"Anne and her journey are a remarkable example of perseverance and extraordinary timing," says Dr. Matulonis.

Today, Sandstrom is doing well. A singer-songwriter, she performs with her husband at venues around Boston.

This is a summary of a longer article at <http://blog.dana-farber.org/insight>.

Digital Healthcare Apps Bring Patient Care to a Screen Near You

Today's digital technology enables physicians at the Susan F. Smith Center for Women's Cancers to extend patient care beyond its doors. Two of the center's oncologists recently led development of innovative digital applications for two different research studies.

The new apps (one web-based and one phone-based) will empower patients with breast and gynecologic cancers to monitor and report symptoms to their care team, tap online resources for information, share concerns and track physical activity.



HOPE (Helping Our Patients Excel) Trial

The HOPE study is a proactive smartphone app designed to improve patients' symptoms and quality of life while on chemotherapy. "Smartphones are the one thing people won't leave home without," says Alexi Wright, MD, MPH, the trial's lead investigator.

"So we're harnessing this tool to help patients manage their symptoms when they are away from us."

The HOPE app reaches out every day and asks patients questions about the symptoms they are experiencing. The app provides tailored information and advice, shares their responses with their care team, and offers advice about whether to contact their physician. In the first study of HOPE, the app was paired with a Fitbit and piloted in 10 patients over a 30-day period. During this time two patients experienced concerning symptoms that were successfully managed at home, saving them unnecessary nights in the emergency department.

For the six-month trial, the PIs are recruiting patients at Dana-Farber as well as rural oncology clinics in New Mexico and South Dakota. The trial will use the HOPE app to collect active participant feedback, and Fitbits to gather passive data about patients' physical activity. The Fitbit not only prompts patients to be more active but also can alert the care team to a significant change in daily step count that may reflect a larger health problem.

"Right now medicine is more reactive than proactive," says Dr. Wright. "One of my hopes for digital health is that we will be able to engage patients as true partners

with their care team and give them the tools they need to live better lives."



YES (Young, Empowered and Strong) Portal

The YES portal is an exciting next step of Young & Strong: The Program for Young Women with Breast Cancer, which focuses on the unique needs of women diagnosed under age 45 with breast cancer.

"These women are not only more technologically savvy, but they're also very busy," says Ann Partridge, MD, MPH, a Dana-Farber breast oncologist and director of the Young & Strong program. "Coming to a support group or workshop is challenging. If you can help them online, it's often a better fit for their needs."

The YES pilot study will register 30 patients – 10 survivors, 10 in early treatment, and 10 in metastatic treatment – to access to the portal, a members-only website, for three months. Participants will fill out questionnaires about their symptoms and what information they'd like to receive. From there they can delve deeper into a resource library, find peer support in a chat room, and chronicle how they feel in a journaling area. They'll also receive emails with inspirational thoughts and self-care reminders. "The goal is to provide more supportive care, education and resources for their symptoms and unique concerns," Dr. Partridge says. "We also hope to connect young women with research opportunities tailored to their needs through the portal."

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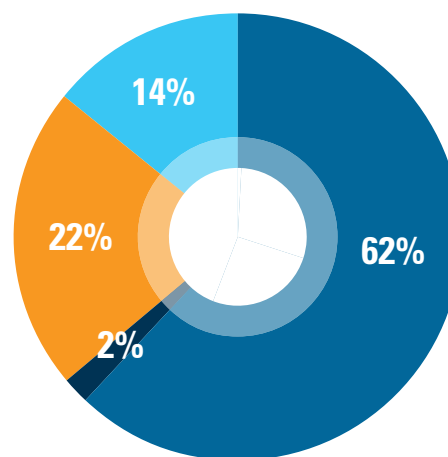
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Susan F. Smith Center for Women's Cancers Executive Council

The Executive Council is guided by a commitment to eliminating breast and gynecologic cancers through education, advocacy, and fundraising. The council dedicates all funds raised for immediate use to the Susan F. Smith Center in pursuit of ongoing breakthroughs in women's cancers research. Founded in 2003, members of the council have, to date, raised more than \$18 million for the Susan F. Smith Center. To learn more about the Executive Council, contact Maryann Zschau at [617-632-5461](tel:617-632-5461) or Maryann_Zschau@dfci.harvard.edu.

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Thanks to the ongoing generosity of our donors, the Susan F. Smith Center for Women's Cancers at Dana-Farber has raised more than \$195 million over the past 20 years, and more than \$30 million in fiscal year 2018 alone. To learn more about how you can strengthen our ongoing work against women's cancers, contact Suzanne Kouri at [617-632-4055](tel:617-632-4055) or suzanne_kouri@dfci.harvard.edu.



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