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JOHNS HOPKINS

BREAST MATTERS

KIMMEL CANCER CENTER

Immune Therapy
Promising for Breast Cancer

A Collaboration with the Bloomberg~Kimmel Institute for Cancer Immunotherapy

Leslie, Immune Therapy Patient

JOHNS HOPKINS MEDICINE

Immune Therapy
Promising for Breast Cancer

Immunotherapy—cancer treatments that empower the body's own natural defenses—is at last becoming a reality and providing unparalleled, long-lasting responses across many cancer types, even in the most advanced and treatment-resistant cancers.

For cancer immunology and breast cancer expert **Leisha Emens**, who has focused her career on developing immune-based treatments for breast cancer, this is the moment she has been waiting for. Recent advances in new immune therapies that block immune checkpoints and the promise of combination immunotherapy strategies are changing the cancer treatment landscape.

This progress is built upon 30 years of discoveries by Kimmel Cancer Center scientists, like **Drew Pardoll** and **Elizabeth Jaffee**, who have painstakingly deciphered the mechanisms of the immune system to reveal how it works and, perhaps more importantly, why it all too often has not worked against cancer. Jaffee's breakthrough discoveries in immune therapy led to her selection as co-chair of Vice President Joe Biden's Cancer Moonshot Blue Ribbon Panel. The Kimmel Caner Center's groundbreaking immunology research and clinical translation are now being fast-tracked as a result of the new Bloomberg~Kimmel Institute for Cancer Immunotherapy at Johns Hopkins. Jaffee, who is an associate director of the institute, plans to use some of these new funds to advance promising translational research in breast cancer. "Until now, there has not been the intense effort at developing immunotherapy for breast cancer. That is about to change," says Jaffee.

The tantalizing opportunity to transform cancer to a chronic disease that patients can live well with has energized cancer scientists and patients alike. "These are very exciting times. Engaging the immune system to fight breast cancer is a game changer," says Emens. "We've never been so encouraged about a cancer treatment strategy. It has remarkable potential."

> "FOR MANY PATIENTS, WE ARE TURNING BREAST CANCER INTO A **CONTROLLED MEDICAL PROBLEM**, LIKE HIGH BLOOD PRESSURE. IMAGINE WHERE WE COULD TAKE THIS IN FIVE YEARS." **–LEISHA EMENS**

Scientists believe they now understand how to give the immune cell the upper hand over the cancer cell. These advances come after years of a cat-and-mouse game where investigators developed immune-based approaches, only to have them thwarted by the cancer cell.

A Major Breakthrough

The major breakthrough came in the discovery of an immune target called PD-1 and a related partner protein on tumor cells called PD-L1. PD-1 is what immunology experts call an immune checkpoint. Laboratory research and early clinical trials point to it as one of the strongest influencers of an immune response to cancer identified so far. PD-L1 can cloak the tumor and is largely responsible for cancer's ability to avert an immune attack.

The body has a system of immune checkpoints to help regulate an immune response. These checkpoints help initiate an immune reaction to abnormal cells, viruses and bacteria. Just as importantly, they help shut down the immune response when the threat has been eliminated. Cancer cells hijack this process to maintain their own survival and turn off the immune response before it can go to work against the cancer. Drugs that block cancer cell signaling to checkpoints, such as PD-1 and PD-L1, are having promising results in some patients, unleashing an immune assault against their cancers.

From left, Evanthia Roussos Torres, Elizabeth Jaffee, Roisin Connolly and Vered Stearns

Members of the Kimmel Cancer Center Breast Cancer Program are leading the way in breast cancer studies of a drug that targets PD-L1. Emens led the first multicenter study in advanced triple-negative breast cancer with the immune drug alone. Six of 37 patients treated survived at least 24 weeks without disease progression, an unusual result among patients with this type of advanced and resistant cancer. Two patients saw their cancers disappear, and tumors shrunk in another two patients.

The promising results in advanced and treatment-resistant breast cancers led to a new, global study of PD-L1 blockade therapy as part of the first line of treatment for metastatic disease, with the goal of gaining FDA approval of the drug as a standard therapy for breast cancer.

Better in Combination

Although the therapy is powerful alone in some patients, Emens and colleagues believe it will work even better, and in more patients, when used in combination with other therapies.

Emens is exploring the anti-PD-L1 drug in combination with drugs that target and inhibit other immune-suppressive factors in the tumor. Her most recent studies focus on inhibitors of an immune checkpoint called IDO and the adenosine pathway, both of which act as an off switch for cancer cell-killing immune T cells.

These trials focus on triple-negative breast cancer because there are few options for these patients, says Emens. "We need newer and more targeted therapies for these women," she says. In addition to the need, triple-negative breast cancer also has features that make it a likely responder to immune therapy.

Triple-negative breast cancer has higher numbers of gene mutations, and these changes to the DNA may make it more recognizable to the immune system. Triple-negative breast cancer also tends to express PD-L1 and has higher numbers of tumor-infiltrating lymphocytes, or TILs. TILs are white blood cells that have left the bloodstream and entered the tumor, a action indicative of an immune response. "It suggests that these cancers are poised for an immune response and would be amenable to immune therapy," says Emens.

Breast cancer expert **Roisin Connolly** was given a Young Investigator Award from the National Comprehensive Cancer Network to dig deeper into this and figure out why and how the immune system acts against breast cancer. With additional funding from the National Cancer Institute and Lefkofsky Family Foundation, Connolly and Breast Cancer Program Director Vered Stearns have been developing combined epigenetic and immune therapies for breast cancer. Epigenetic therapies target alterations in the chemical environment of DNA that promote cancer development. Recent preclinical studies from breast cancer laboratory scientists, including young investigator **Evanthia Roussos Torres**, led Connolly and Stearns to a combined epigenetic/immune checkpoint therapy approach that works in synergy against breast cancer.

Connolly is studying the value of giving an epigenetic drug known as a histone deacetylase inhibitor, or HDAC inhibitor, for two weeks before adding agents that target the immune system. Connolly, Stearns, Torres and Jaffee are studying tumor biopsies and blood samples obtained from patients with hormone receptor-positive and triple-negative breast cancer to identify biomarkers that will help distinguish patients who will respond best to these treatments.

Promise for All Breast Cancers

Emens is also looking beyond triple-negative breast cancer, exploring immune approaches in essentially every type of breast cancer. In breast cancers that express the HER2 protein, known as HER2-positive breast cancer, she is studying anti-PD-L1 checkpoint blockade in combination with a drug that targets the HER2 gene, a known driver of breast cancer development. She is also studying the value of adding the immune drug to antibodies that target and block HER2 from fueling the growth of cancer cells.

"HER2-directed antibodies already have very interesting immune-based effects," says Emens. "There is huge potential for synergy."

Emens says triple-negative and HER2-postive breast cancers tend to be inflamed, which indicates they have already attracted cancer-killing immune T cells. "That makes them great candidates for checkpoint blockade," says Emens. "For tumors with T cells in them, checkpoint blockade therapy unleashes the immune activity."

"THE POTENTIAL TO USE IMMUNE THERAPY LOOKS GREAT, AND **IT IS ONLY GOING TO GET BETTER** WITH MORE RESEARCH."
–LEISHA EMENS

A Vaccine

The challenge, Emens says, is that there are many breast tumors that do not have T cells in them. "We have to do something to attract the T cells," she says. She has just the thing in her aresenal—a vaccine that calls T cells in record numbers to cancers. It is called GVAX. Developed by Jaffee, it recruits the vital T cells, which are manufactured by our own body and are immensely more powerful than any anticancer drug. If the vaccine is integrated with checkpoint blockade—to circumvent the cancer cell's immune suppressing capabilities—Emens believes they could obtain immune responses against virtually every type of breast cancer.

Currently, however, trials to test this theory are on hold as Emens tries to raise the funds needed to manufacture the vaccine. "The time is right. We have the opportunity to impact a lot of people. Funding is the challenge," she says.

Most cancer experts agree that there has probably never been another time when so many promising opportunities were within scientists' grasp. Unfortunately, this time converges with a significant tightening of federal funding available for cancer research.

Members of the breast cancer and immunology programs at the Kimmel Cancer Center are working closely together to secure funding to conduct clinical trials of checkpoint blockade combinations with other promising agents or vaccines.

From Treatment to Prevention

Ultimately, Emens hopes breast cancer vaccines can be used to prevent breast cancer recurrence or even keep high-risk patients from developing breast cancer in the first place. "What does the immune system do? It keeps you from getting sick. That's what a vaccine does, and we have a vaccine," says Emens. She is launching a project to characterize the molecular changes that drive breast cancer. Once they are understood, the vaccine could be targeted to shut down specific molecular influencers of breast cancer development.

"The potential to use immune therapy looks great, and it is only going to get better with more research," says Emens. "We are on the brink of major breakthroughs. PD-1 was one major advance, and now we have to move on to the next one, and the next one, and the next one."

Her inspiration comes from the many breast cancer patients she has treated. The patients who have received immune therapy are small in numbers right now, but some have experienced huge benefits from immune therapy. "I have some patients who have been on immune checkpoint blockade for a couple of years and are doing great," says Emens.

Leslie is one of these patients. "Facing my second bout with breast cancer, I felt my approach to this battle needed to be strategic. My faith, Johns Hopkins and immune therapy provided a solid recovery platform that has empowered me to enhance my prospective on living a full life," says Leslie, a triple-negative breast cancer patient treated in one of Emens' immune therapy clinical trials.

"But for immune therapy, so many of these patients would have been on multiple types of chemotherapy and probably gotten sicker and sicker. Instead they are having great quality of life. For many patients, we are turning breast cancer into a controlled medical problem, like high blood pressure. Imagine where we could take this in five years," says Emens.

"**WE ARE IN A NEW ERA.** CANCER TREATMENT HAS MOVED FROM TOXIC THERAPIES THAT ARE NONSPECIFIC TO AN AGE WHERE TARGETED THERAPIES DO A BETTER JOB OF CONTROLLING CANCER WITH FEWER SIDE EFFECTS." **–ELIZABETH JAFFEE**

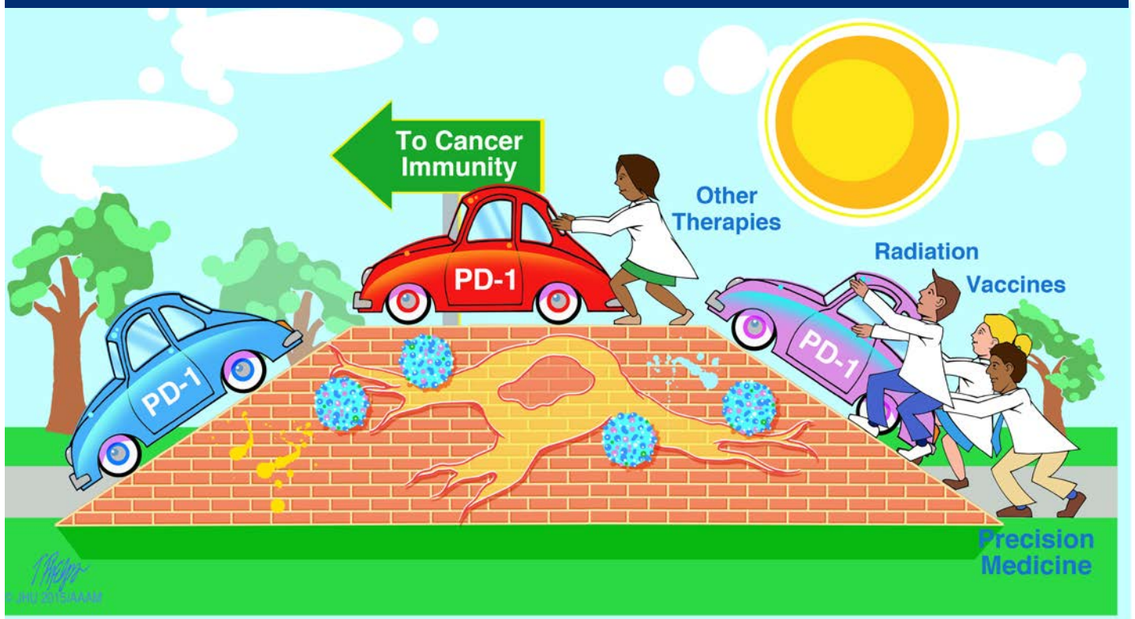
A New Era

The breast cancer group is conducting extensive laboratory investigations and plans to launch larger projects with initial support from the Bloomberg~Kimmel Institute for Cancer Immunotherapy.

"We are in a new era. Cancer treatment has moved from toxic therapies that are nonspecific to an age where targeted therapies do a better job of controlling cancer with fewer side effects," says Jaffee. "Immunotherapy is the ultimate targeted therapy and has already had some success in treating breast cancer. Dr. Stearns and her breast cancer team are committed to turning breast cancer into an insignificant problem for all women, and one important way we will accomplish this is by continuing research to develop and refine interventions that activate each woman's immune system to eradicate and ultimately prevent breast cancer." ■

Research nurse Maureen Berg, Leslie and Dr. Leisha Emens

THE ROAD TO CANCER IMMUNITY: "IF A CAR IS SITTING AT THE TOP OF A HILL WITH THE FRONT POINTING DOWNHILL, IT MAY ONLY NEED THE PARKING BRAKE RELEASED TO START MOVING. ANOTHER CAR SITTING ON A FLAT ROAD MAY NEED THE BRAKE RELEASED AND A PUSH TO GET GOING. A CAR SITTING AT THE BOTTOM OF A HILL AND FACING UPHILL WILL NEED THE BRAKE RELEASED AND A LOT OF GAS TO GET MOVING," SAYS DREW PARDOLL, DIRECTOR, THE BLOOMBERG~KIMMEL INSTITUTE FOR CANCER IMMUNOTHERAPY



Beyond Breast Cancer

A dedicated breast cancer team, unwavering in its quest to advance discovery and clinical advances for women fighting the disease, leads to inspirational patient stories of hope and survivorship.

DEVON'S STORY

Overcoming anxiety and fertility challenges, Devon becomes a breast cancer survivor and a mother of twins.

It was the summer of 2013, and Devon Conklin was at an exciting juncture in her life. Her career as a dentist was taking off. She was married to a man she loved deeply, and they were planning to start a family. In fact, Devon and her husband, Kyle, had recently decided that she would begin in vitro fertilization (IVF) after their attempts to become pregnant naturally had failed. Then one day, as she was relaxing at home watching TV, Devon discovered a lump on her breast. It was small, only the size of a pea, but wisely, she didn't ignore it.

Immediately, Devon made an appointment with her reproductive endocrinologist. "She said it was nothing, probably a cyst. She told me to wait until after my period, that it was probably hormonal," Devon recalls. The advice did little to comfort Devon, who was persistent in getting a biopsy ordered.

Altered Reality

Shortly after the biopsy, the 30-year-old was shocked to learn she had cancer. She'd been diagnosed with invasive ductal carcinoma, a common form of breast cancer that originates in the milk ducts. Along with the new diagnosis, Devon received some good news: The doctor was fairly certain that the cancer was stage l. Nevertheless, she was forced to make a quick decision about her future.

Prior to receiving her cancer diagnosis, Devon and Kyle had decided to proceed with IVF therapy. Devon's doctor advised her to begin taking the fertility drugs before starting treatment for breast cancer. So just a week before undergoing a lumpectomy to remove the small tumor from her breast, Devon harvested 10 eggs, three of which were successfully fertilized. Between her surgery and the few months later when she began chemotherapy, Devon underwent a second effective egg retrieval.

Although Devon's cancer prognosis was good and she was progressing well with treatment for both her cancer and infertility, she was wracked with fear about her future. "I was a mess. My brain went to the worst possible situation," Devon acknowledges. But that didn't stop her from choosing the least invasive surgery. She opted for a lumpectomy versus a mastectomy (complete removal of breast tissue) after learning that the outcomes for patients with her type and stage of cancer were statistically similar. "I thought maybe I could breast-feed," Devon says; again, thinking of her future.

An Eye Toward the Future

After the lumpectomy, Devon proceeded with chemotherapy and radiation treatment.

In 2014, with most of her treatment behind her, Devon once again began to turn her attention toward having a baby. Ovarian suppression drug therapy was part of her breast cancer therapy and results in the temporary onset of menopause, so carrying a pregnancy was not a possibility for Devon. She started considering finding a gestational carrier. Devon shared her thoughts with her medical oncologist, **John Fetting**, who encouraged her to learn more about the process.

Devon followed Fetting's suggestion, speaking with a surrogacy attorney, contacting surrogacy agencies and, finally, meeting a woman via word of mouth who was interested in becoming a gestational carrier—someone who carries the fertilized egg of another woman.

The want-to-be carrier lived in Baltimore and already had two children of her own. The two women immediately forged a bond, and in August 2015, two of Devon's fertilized eggs were implanted into the gestational carrier's womb. Nine months later, she gave birth to Devon and Kyle's two adorable twin boys, Holden and Brooks.

Coming Full Circle

It's been a whirlwind three years for Devon from the chance discovery of a pea-sized lump to the birth of her twin sons. There remain reminders of her cancer: Devon sees her surgeon twice a year, has a mammogram and an MRI scan annually, and receives a monthly injection of hormone-based therapy goserelin, aimed at preventing her cancer from coming back.

It's only natural that she sometimes worries about the future and the cancer coming back, but she says she tries to follow in the footsteps of those who served as a motivating force while she was in the midst of treatment. "I've grown, learned to cope with things," Devon says. "I had several amazing women who were diagnosed before me and who have been a huge encouragement to me." She counts the Kimmel Cancer Center's **Jill Mull**, a navigator for young breast cancer survivors, as one. Mull is also a breast cancer survivor and mother of twins.

Like those who inspired her, Devon has begun sharing her story with other breast cancer patients. "I'm finally getting to the place where I can talk to other women about it now. I love that," Devon says.

Kyle and Devon Conklin with their twins, Holden and Brooks

GRACE'S STORY

A supportive medical team, strong faith and impressive physical stamina mark Grace Ligon's journey with cancer.

Grace Ligon was just 13 when her mother died of breast cancer. Then, in her mid-40s—when she was just about the same age as her mother when she died from the disease—Grace found a lump in her breast. That day marked Grace's own personal odyssey with breast cancer.

High Praise for Her Medical Team

Grace's initial breast cancer diagnosis in 2000 and subsequent treatment, while rigorous, was fairly standard: a lumpectomy, followed by six months of chemotherapy, then six weeks of radiation and five years of tamoxifen. But, she says, the members of her Kimmel Cancer Center medical team were anything but standard. She calls her surgeons, **Martha Zeiger** and **Lisa Jacobs**, "wonderful." Recalling a conversation with her medical oncologist, **Antonio Wolff**, to discuss the best treatment options for her, she describes him as "simply amazing."

"All of my doctors at Johns Hopkins have been amazing. I trusted them. I felt heard," says Grace, who describes herself as a "fairly compliant" patient but admits that she'll speak out when she has a concern about something.

This was the case when she began taking aromatase inhibitors, drugs that block the cancer-fueling hormone estrogen. The class of drugs was relatively new at the time of Grace's diagnosis and could provide some protection against cancer recurrence. Although she wanted to do all that she could to prevent her cancer from coming back, her quality of life was being impacted by significant side effects from the drugs. Consulting with Wolff and carefully weighing the small potential benefits with the serious side effects she was experiencing, they decided to remove the drugs from her treatment plan. "I wanted to feel healthy enough to resume competitive physical activities. That was very important to me," she says.

Stamina in the Face of Setbacks

In 2006, the Columbia, Maryland, resident learned of an inaugural Iron Girl triathlon, for females only, being held in her town. "I told my husband, this is what I want to do for my 50th birthday."

While Grace had always been a recreational runner and swimmer, training for and competing in a triathlon would be a significant undertaking, particularly after the rigorous and fatigue-inducing cancer treatment she'd recently undergone. In 2007, Grace successfully completed her first triathlon. Since then, she's competed in at least one triathlon a year, calling it a lifesaver, mentally.

In 2011, her annual triathlon was put on hold when her mammogram showed

calcifications on the same breast that she had the lumpectomy. These small calcium deposits are common and usually benign. A biopsy showed, however, that it was, in fact, cancer, and after consulting with Wolff, Jacobs and the entire multispecialty Breast Cancer Program team, she proceeded with a mastectomy.

The following year, Grace felt a tiny mass below her clavicle. A bone scan determined that her breast cancer had spread to her sternum. She remains hopeful and undeterred. She receives monthly injections of hormonal therapy to keep the cancer in check and says it worked, keeping it "fairly stable" since 2012. "I'm a pretty healthy cancer patient. I tell people I'm a person living with cancer," says Grace.

Finding Strength Through Faith

She has special inspiration in her battle with cancer. Both of her children were born with a rare, inherited genetic disease that causes vision problems and can potentially lead to blindness. Grace and her husband have been buoyed by the promise of emerging research coming out of the Johns Hopkins Wilmer Eye Institute, where their children have been seen for several years. Grace credits her strong faith with the ability to continue moving forward, in spite of her family's health challenges.

Grace also finds solace and strength in the public expression of her faith. After a hiatus from singing in the choir at her local church, she resumed her membership in 2011. Grace says the choir has been like a support group for her.

"Cancer can feel so isolating. Just to have the experience of connecting with other people through worship music, by singing with one particular purpose, has a powerful physiological effect," Grace says.

She points to a British study that found that choral singing increased levels of immune proteins, reduced stress and improved mood.

Grace finds strength in all aspects of her life. The wife, mother, triathlete and choir member also works professionally as a psychotherapist. She says her work has made her aware of her own personal strength, and her cancer battle has given her perspective and insights that, she believes, enable her to better advise her own patients in their unique struggles.

Grace is confident that she has the best breast cancer experts working to keep her cancer in check, and she credits them for helping her keep her positive outlook throughout the ups and downs of her cancer journey. She continues to compete in triathlons and learned that Wolff competed in one of the same events. "It's pretty special to be able to high-five your oncologist and compare notes about such a grueling physical competition," says Grace.

"Feeling heard, feeling respected, being able to question when I didn't understand things—this has been really helpful," says Grace. "When facing a disease like cancer that makes you feel so out of control, having a team like this working for me has made all of the difference."

"FEELING HEARD, FEELING RESPECTED, **BEING ABLE TO QUESTION** WHEN I DIDN'T UNDERSTAND THINGS—THIS HAS BEEN REALLY HELPFUL."
–GRACE LIGON

Grace Ligon

ERIN'S STORY

Stage 2 cancer derailed Erin Yale's dreams of growing her family. But it did not stop her from continuing to be a loving mother and dedicated professional, as well as the founder of a nonprofit that inspires people to make healthy lifestyle choices and reduce their risk of cancer.

Erin Yale nursed her 4-month-old daughter for the very last time while waiting in a doctor's office for the results of a biopsy taken from her breast. When results showed that Erin had breast cancer, she decided against continuing the nurturing practice that was just one of the many aspects of new motherhood that she had embraced. In fact, Erin took so readily to motherhood that she and her husband began talking about when they'd have more children soon after she gave birth to their first. Then suddenly, their discussions shifted jarringly to talk of cancer treatment.

For the new mother and career-oriented young woman—Erin's career at global financial giant Legg Mason was taking off—nothing could have come as a greater shock. And yet, there had been some warning signs.

The Lump

A year before her diagnosis, Erin had detected a lump in her breast. She received a mammogram, followed by an ultrasound, which showed some dense tissue mass. The health care provider dismissed the vague results, even after Erin shared information about her family's history: Her grandmother and aunt on her father's side had breast cancer. Subsequently, they would also test positive for a gene mutation linked to breast cancer, as would her father, sister and Erin.

But originally, Erin tried to dismiss the family link. "I was naive in thinking that because I had two older sisters who didn't have breast cancer, I wouldn't get it, especially since I was only in my 30s," Erin says.

Then, a year later, when breast-feeding her newborn, Erin noticed the lump was getting bigger. Even when she made an appointment to get a biopsy of the lump, the surgeon at the local hospital who performed the procedure told her not to worry—he didn't think it was cancerous.


Steve and Erin Yale and daughter

The Shocking News

The biopsy showed Erin had stage 2 breast cancer, which had spread to her lymph nodes. Erin's initial reaction was total shock and surprise. "It was overwhelming. Instead of focusing on being a new mom, I had to deal with all these other things," she recalls. Erin credits her husband with providing strength and support at a time when she needed it most. He researched doctors, treatments and related information about breast cancer.

Toward Recovery

Soon afterward, they found themselves at Johns Hopkins. Erin says she "absolutely loves" her oncologist, **John Fetting**. She says he always sits at eye level when he speaks to her. She appreciates his thoughtfulness—he often inquires about her and her family—and the general concern he demonstrates.

Similarly, Erin expresses strong satisfaction with the other health care providers on her medical team. Of her radiation oncologist, **Fariba Asrari**, Erin says: "She always gave me hugs when I saw her. She was so happy and encouraging." Erin also appreciates the responsiveness of the chemotherapy nurses, who always promptly responded to her phone calls and questions.

The supportive nature of Erin's medical team didn't eliminate the difficult and lengthy treatment process she endured, but it certainly made it more bearable. After a lumpectomy, Erin underwent six months of chemotherapy and 28 rounds of radiation. After her chemotherapy regimen was completed, Erin had a bilateral mastectomy.

Throughout Erin's treatment process, the unyielding support of family and friends helped sustain her. She recalls her girlfriends making a "chemo basket" of small wrapped gifts that she'd open when she needed a boost. She decided against joining a formal support group, choosing instead to spend her free time at home with her daughter and husband.

Now her little girl is 5 years old, and Erin—having successfully completed treatment—is back at her busy life, full throttle.

"I TRY TO STAY POSITIVE, TO KEEP THINGS IN PERSPECTIVE," SHE SAYS. "**I STAY FOCUSED ON WHAT'S IMPORTANT**—LIKE THE FACT THAT I HAVE A BEAUTIFUL, HEALTHY DAUGHTER." **–ERIN YALE**

Pushing Pink Elephants

In addition to being a mom, Erin juggles a demanding job in management at Legg Mason. And in whatever spare time she can muster, she tends to a nonprofit she co-founded in 2012. The organization, Pushing Pink Elephants, began as a blog that Erin wrote to keep friends and family informed of her cancer status and treatment plan. Out of that came a broader goal of bringing cancer awareness and prevention to the general public through education, resources, and partnering with local cancer treatment and support organizations. In just four years, the nonprofit has grown to include five board members, each committed to promoting cancer awareness and inspiring consumers to make healthy lifestyle choices.

While Erin has exhibited impressive strength and resiliency throughout her journey with cancer, she acknowledges that it hasn't always been easy. "Sometimes I struggle and think that I just want to be a normal 35-year-old person," says Erin, who has had to come to terms with closing the door on having more children, which is particularly difficult when so many of her peers are growing their families.

"I try to stay positive, to keep things in perspective," she says. "I stay focused on what's important—like the fact that I have a beautiful, healthy daughter." ■

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Breast Cancer Expertise and Care Expands

Sept. 7, 2016, marked the formal opening of the Sidney Kimmel Cancer Center at Sibley Memorial Hospital, located on the Johns Hopkins national capital region campus.

The Sidney Kimmel Cancer Center at Sibley brings innovative cancer treatment, advanced research and nationally recognized experts to the Washington, D.C., region," says **William Nelson**, Johns Hopkins Kimmel Cancer Center director. The new center at Sibley includes a new clinical building and expansion of experts, medical oncology facilities, and services to Sibley's Sullivan Breast Center.

The Sullivan Breast Center is a multidisciplinary and comprehensive program with breast surgeons, medical oncologists, radiation oncologists, radiologists, pathologists, geneticists, nurse navigators and other practitioners on-site and working in full collaboration with colleagues at the Kimmel Cancer Center's Johns Hopkins Hospital site in East Baltimore.

"The cancer care is state of the art at all Kimmel Cancer Center sites," says **Maureen O'Donnell**, a breast surgeon who trained at The Johns Hopkins Hospital and Sibley. She joins breast surgeon and program director **Colette Magnant**, who started the breast center at Sibley in 1998. "Sibley provides the same excellent care as the Kimmel Cancer Center in East Baltimore," says O'Donnell.

Magnant is the core of the Sibley breast cancer program. She is credited with establishing the multidisciplinary care structure.

The center is named for one of her patients, Rachel Sullivan, who was 35 and pregnant when she was diagnosed with breast cancer. She calls Magnant an angel. Sullivan says Magnant guided her to the best therapies. Fifteen years later, she remains cancer-free. In 2006, she and her husband, Tom, donated the naming gift in Magnant's honor.

Vered Stearns and Colette Magnant

"I can't say enough about how wonderful Dr. Magnant is. She's incredible," says Sullivan. "My husband and I funded the breast center to give back to her. It was her vision and her dream. I wish it was her name on the building." She encourages other patients to give back to their doctors and care team by supporting programs and making contributions, if they are able.

For Magnant, the focus has always been on patients, and she sees the latest changes as a way to bring excellent care to more patients. "We have seen a lot of growth over the years, and I am very excited about the new expansion," she says.

Magnant says her team sees a lot of patients under 40. With this young age at diagnosis comes special needs, and the Sullivan Breast Center also has several unique services directed at younger patients, including a genetics specialist, access to fertility preservation and a dedicated support group for younger patients.

"I am excited about what we've accomplished and our vision for this expansion," says Magnant. She enjoys collaborating with Kimmel Cancer Center Breast and Ovarian Cancer Program Co-Director **Vered Stearns** on ways to grow the program. "She and her colleagues have so many ideas. We are already looking to the next phase," says Magnant. "We are all focused on continuing the great care we provide to patients and enrolling patients in clinical trials so we can figure out what therapies might work better."

Clinical Research

The addition of clinical trials comes with the expansion of medical oncology at Sibley, led by medical oncologist **Karen Smith**. She has been at Sibley for three years and, in collaboration with her colleagues in surgery and radiation oncology, has opened more than 25 clinical trials. "The vast majority of clinical trials that are available to breast cancer patients in East Baltimore are now also available at Sibley. My goal, over time, is to grow that from most trials to all trials," says Smith. Medical oncologist **Raquel Nunes** joined Smith in September to expand the breast cancer medical oncology team at Sibley.

Like her other Sullivan breast center colleagues, Smith is a full member of the Kimmel Cancer Center breast program. All of the Sibley-based experts participate in multidisciplinary conferences to review patient cases at Sibley and at The Johns Hopkins Hospital.

The expansion of the Sibley program reflects a growing need in the Washington, D.C., area. The Sibley site treats about 450 new breast cancer patients a year, and the addition of clinical experts and clinical research will support continued growth and access to the most advanced breast cancer treatments.

The multispecialty team at Sibley's Sullivan Breast Center

It is a seamless extension of the Kimmel Cancer Center Breast Cancer Program, says Smith. "It offers comprehensive care for breast cancer patients in the Washington, D.C., area through the Johns Hopkins system," she says. "We are one system, and we have set it up that way. If necessary, a patient could get one part of their treatment at Sibley and another in East Baltimore."

Advanced Care and Technology

The Sullivan Breast Center has all of the same technology—3-D mammography, MRI, MRI-guided biopsy, state-of-the-art breast imaging and the most advanced pathology. The expansion of the breast center team coincides with the completion of the new Johns Hopkins Sidney Kimmel Cancer Center at Sibley that brings together a wealth of advanced resources, including private infusion rooms, the latest radiation oncology techniques, top surgical expertise, clinical trials, social work and a host of support services.

"We have the highest-quality care in both locations, but one of the nice things about Sibley is that it's a little bit smaller and easier to navigate for patients," says Smith.

Other experts joining the Sullivan Breast Center team include renowned pathologist **Andrea Richardson**. She comes to the Sibley team from Dana-Farber Cancer Institute to lead the breast pathology and anatomical pathology program. Richardson has specialized in breast pathology for more than 20 years and splits her time between Sibley and East Baltimore, where she collaborates with Kimmel Cancer Center breast cancer expert **Ben Park** on laboratory research. She presents the pathology at the breast cancer multidisciplinary clinics and oversees the breast cancer tumor board at Suburban Hospital, another growing Kimmel Cancer Center site.

Richardson is excited about a $120,000 telepathology system funded by Kimmel Cancer Center advisory board member Peter Kovler that connects Johns Hopkins, Sibley Memorial, Suburban and Howard County General hospitals via video microscopy. "The system brings together all Johns Hopkins pathology efforts. It transmits images in real time as we move slides to look at different parts. The people at other locations can see exactly what the person looking through the microscope is seeing," says Richardson. "It allows us all to do things in a similar way across all of the hospitals. When we encounter an unusual case, we can show it to our colleagues in East Baltimore and draw upon their expertise."

Radiation Oncology

Jean Wright is heading up the breast radiation oncology expansion at Sibley and Suburban, as director of breast radiation for the Johns Hopkins Department of Radiation Oncology and Molecular Radiation Sciences. The Sibley and Suburban hospital radiation oncology centers have the same equipment as the East Baltimore site, with new machines and all of the technology necessary to provide patients the most advanced radiation therapies, including prone radiation and breath hold techniques. In addition to integrated technology, the specialized medical physics and dosimetry teams at Sibley, Suburban and in East Baltimore often collaborate with radiation oncologists on all Johns Hopkins campuses and have developed standardized practices across all sites.

"Facilities are the same in all locations, we have the same quality and safety protocols, and we have the same clinical trials," says Wright. "We use a variety of different tools to tailor treatment to each patient's unique scenario." Sibley will also house the Johns Hopkins proton radiation facility, which is under construction and anticipated to be operational in 2019. Protons may benefit selected breast cancer patients, and Wright is planning several clinical trials involving protons that will further enhance our capabilities in treating breast cancer with radiation.

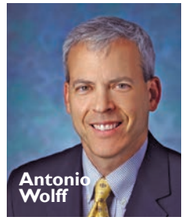
Come to Sibley

"Everyone is excited. We already had a great comprehensive program for women with breast cancer, and now we are adding experts and expanding facilities to make it even better," says Magnant. "We can now say to all patients, 'If you have breast cancer and you live in the Washington, D.C., area, come to Sibley. We'll take care of you.'" ■

Genetic Test

A guide for treatment of early breast cancer

In the era of molecular medicine, the absence of genetic alterations, such as hormone receptor status (HR-positive or -negative), play an essential role in guiding treatment decisions for patients with breast cancer. They are particularly useful in uncertain cases, helping to direct therapy to those who will benefit but sparing those who do not need additional treatment. In breast cancer, several genetic biomarkers—HER2, ER (estrogen receptor) and other markers—help stratify risk and tell clinicians what therapies are likely to work, and more importantly, which therapies will not. Gene expression profiling (GEP) is another tool used to guide post-surgery treatment decisions in early-stage breast cancers that are hormone receptor-positive but have not spread to the lymph nodes. Experts know that some of these patients are cured with surgery, but some will see their cancers recur and spread.



A multispecialty research team, led by **Antonio Wolff** and biostatistician **Leslie Cope**, developed a model that uses predictors of cancer recurrence. They released a web-based application that helps doctors decide if additional complex molecular testing is needed to complement pathology information to guide treatment decisions and help improve results for early-stage breast cancer patients.

Molecular Tool

"Liquid biopsy" may identify therapeutic targets

A new powerful technique allows researchers to study multiple genetic alterations within a single tumor. It is known as liquid biopsy, because it identifies these gene mutations from blood rather than tissue taken at surgical biopsy, and Kimmel Cancer Center breast cancer experts are conducting studies to determine how the innovative molecular technology might be used to guide therapy. **Ben Park**, **Vered Stearns** and their colleagues studied biopsy tissue and blood samples from 20 women with metastatic triple-negative breast cancer who were making decisions about treatment approaches. The researchers reported that the majority of patients received a treatment recommendation based on the genetic profile of the tumor. They also demonstrated that the majority of mutations that were detected in tumor tissues obtained from surgical biopsy were also seen in blood. These results demonstrate the potential of "liquid biopsies" to determine if tumors cells contain mutations that could be targeted with new treatments.

Triple-Drug Combo for Triple-Negative Breast Cancer

Shrinks tumors and stops cancer growth

A new study using mice and lab-grown human cells showed how a triple-drug cocktail can shrink triple-negative breast cancers by killing off cancer cells and halting new tumor growth. The combination, known as EAD, included the chemotherapy drug doxorubicin; all-trans retinoic acid, which can cause a tumor to lose its self-renewing cells; and entinostat, which makes cancer cells more sensitive to retinoic acid treatment. Lead investigator **Sara Sukumar**, the Barbara B. Rubenstein Professor of Oncology, says EAD significantly reduced the size of triple-negative breast cancer tumors in mice and the number of lab-grown spheres of metastatic breast cancer cells harvested from patients and grown in the laboratory.

How Stem Cells Help Cancer Survive

Low-oxygen breast tumor environment is nursery for cancer stem cells

Working with human breast cancer cells and mice, scientists have undertaken new experiments that explain how certain cancer stem cells thrive in low-oxygen conditions. Proliferation of such cells, which tends to resist chemotherapy and helps tumors spread, is considered a major roadblock to successful cancer treatment. The new research, suggesting that low-oxygen conditions spur growth through the same chain of biochemical events in both embryonic stem cells and breast cancer stem cells, could offer a path through that roadblock, the investigators say. Study leader **Gregg Semenza**, the C. Michael Armstrong Professor of Medicine and a member of the Johns Hopkins Kimmel Cancer Center, says there are still many questions left to answer, but they have shown that oxygen-poor environments, like those often found in advanced human breast cancers, serve as nurseries for the birth of cancer stem cells. The new finding provides possible new targets for drugs to diminish their threat in human cancer.

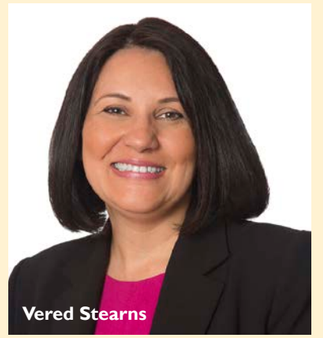
Giant of Cancer

Accelerating approval of new breast cancer drugs

Tatiana Prowell was selected from an elite group of finalists for the 2016 Giants of Cancer Care recognition program. The program honors renowned physicians and researchers who have improved the care for patients and families affected by cancer. Prowell is being recognized for pioneering a novel pathway to accelerated approval for drugs as first-line treatment for high-risk, early-stage breast cancer. Her work resulted in accelerated approval of pertuzumab (Perjeta), which substantially prolongs survival in metastatic HER2-positive breast cancer, to treat patients with early stage HER2-positive breast cancer.

BEAM Study

Shedding light on women truly at risk for breast cancer



"Prevention is better than cure" is an age-old adage, and proven true time and time again with the successful implementation of public health measures with vaccines against most infectious diseases. In each case, their success was due to the fact that they were able to identify who needed it most and administer it to the susceptible population. Cholera vaccines are administered in tropical countries with poor sanitation, and polio vaccine is given to children all over the world. However, for diseases like breast cancer, defining who is at risk is difficult, unless there is an inherited high cancer risk gene in the family or a family history. The majority of women who develop breast cancer do not have any identifiable risk factors. So the first hurdle to overcome for instituting prevention modalities for cancer is to identify those people at high risk of developing the disease.

Breast cancer experts **Lisa Jacobs**, **Nagi Khouri**, **Vered Stearns** and **Sara Sukumar** collaborated with investigators at Northwestern University to find molecular methods that can distinguish between women who are at normal risk and need just routine mammography from those who are a high risk and need additional preventive measures to avoid breast cancer. The current measure of abnormalities in the cells of the normal breast, called cytological atypia, is not quantitative and needs trained experts to read the slides. In their recently published study on BEAM—short for breast estrogen and methylation—they looked for two potential indicators of breast health: the levels of the hormone, estrogen, and methylated genes in the normal breast cells. One of the earliest indications of change when a normal breast cell begins to convert to a tumor cell is methylation, a chemical change to the DNA of a number of important genes.

The team collected cells from the normal breast of nearly 400 women using a procedure called random fine-needle aspiration. These cells were analyzed in the laboratory for the presence of gene methylation. Breast cells from the majority of women showed a "normal" profile, but a substantial number of the women were found to have higher than normal levels of methylated genes in their breast cells. These breast cells with high methylation markers also very often harbored other structural and functional abnormalities, known as cytological changes.

The researchers zeroed in on eight methylated genes—independent of age or menopausal status, risk of developing breast cancer, and breast density—and found that methylation of these genes increased with cytological changes in cells. Their study indicates that increasing methylation of these eight genes could be used as biomarker in assessing breast cancer risk. Sukumar and cancer prevention and control expert **Kala Visvanathan** are conducting additional studies to confirm these results.

Women May Be Able to Reduce Breast Cancer Risk Predicted by Their Genes

How healthy lifestyle choices can mitigate genetic and family history

Women with a high risk of developing breast cancer based on family history and genetic risk can still reduce the chance they will develop the disease in their lifetimes by following a healthy lifestyle, new research led by breast cancer prevention and control expert **Kala Visvanathan** and her colleagues at the Johns Hopkins Bloomberg School of Public Health suggests.

White women who are at high risk but who had a low body mass index (a marker for obesity), did not drink or smoke, and did not use hormone replacement therapy had roughly the same risk as an average white woman in the United States, the researchers found. The average chance that a 30-year-old white woman will develop breast cancer before she is 80 is about 11 percent.

The researchers found that roughly 30 percent of breast cancer cases could be prevented by modifying known risk factors—say, by drinking less alcohol, losing weight and not taking hormone replacement therapy. More importantly, the study found that a larger fraction of total preventable cases would occur among women at higher risk levels because of genetic risk factors, family history and a few other factors that cannot be modified.

The model is still several years from being ready for routine medical use. The researchers also call for development of a model for other ethnic populations and for specific subtypes of breast cancer, which may have different causes and prognostic outlooks. The scientists hope that once women understand that their genes do not completely predict their cancer destiny, they will work even harder to make lifestyle changes that can potentially reduce the risk they will develop the deadly disease.

Magnolia Tree and Breast Cancer Prevention

A compound made from the tree's bark shows promise

Stand under the glossy green canopy of a southern magnolia in full bloom, and you'll be dazzled by this tree's show of hundreds of highly perfumed ivory blossoms, each the size of a teacup. It's a stunning sight, but for centuries, *Magnolia grandiflora* has been known for more than its beauty. The tree contains a pharmacopeia of sorts, yielding chemical compounds that have been used to treat everything from anxiety to heart attack.

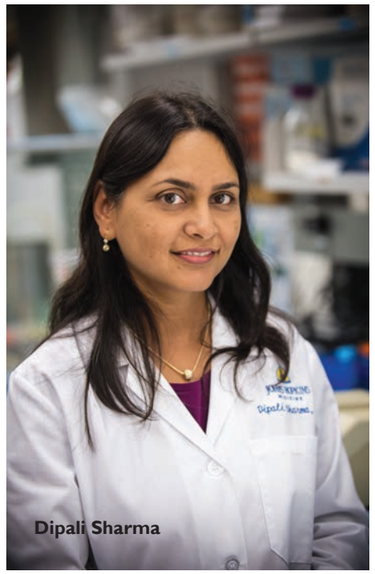
Breast cancer expert **Dipali Sharma** thinks it may be time to add some breast cancers to this list of ailments. With her team at the Kimmel Cancer Center and support from the Fetting Fund and Breast Cancer Research Foundation, Sharma is testing a magnolia compound called honokiol that seems to slow the growth of breast cancers fueled by an excess of leptin, a hormone closely connected with obesity.

Sharma and her colleagues have turned to honokiol after many years of studying the complicated role that leptin plays in breast cancer—and the role of obesity as a risk factor in many cancers. The well-known Million Women Study conducted through the University of Oxford suggested that about half the cancers in postmenopausal women in the United Kingdom can be attributed to obesity. Other studies have found that women at the highest body-mass index (BMI) levels have double the death rate from breast cancer, compared to those in the lowest BMI tier.

With nearly two-thirds of U.S. adults overweight or obese, according to the Centers for Disease Control and Prevention, it's a cancer risk factor that is poised to become "a very significant medical problem," Sharma says. "Developing a preventive and therapeutic strategy for cancer in the obese state is extremely important."

A Hormone's Hyperactive Signals

Leptin is sometimes called the "starvation hormone," although its role in the body is much more complicated. It is made by fat cells and helps to regulate the body's energy stores by suppressing hunger.



Dipali Sharma

People who are obese make more leptin because they have a higher percentage of body fat, but their bodies appear to be resistant to this hunger-inhibiting signal.

Unfortunately, the abnormal increased flow of leptin can trigger a variety of other changes in the body. Sharma and others have shown that leptin and its latchlike receptors on the surfaces of cells are overabundant in breast cancer cells, compared to normal breast cells. Their studies demonstrate that hyperactive leptin signaling by these cells causes the cancer cells to multiply and invade tissue, and spurs the growth of the blood vessels that feed tumors.

"We learned that leptin-induced tumors quickly learn to evade all the usual biological checkpoints that have been put in place to keep the tumors from growing and spreading fast," says Sharma. Leptin helps the tumor cells make a critical change in their shape and mobility, she explains, "and after achieving this state, a tumor cell becomes poised to migrate, invade and transition from a primary, noninvasive tumor to an invasive tumor."

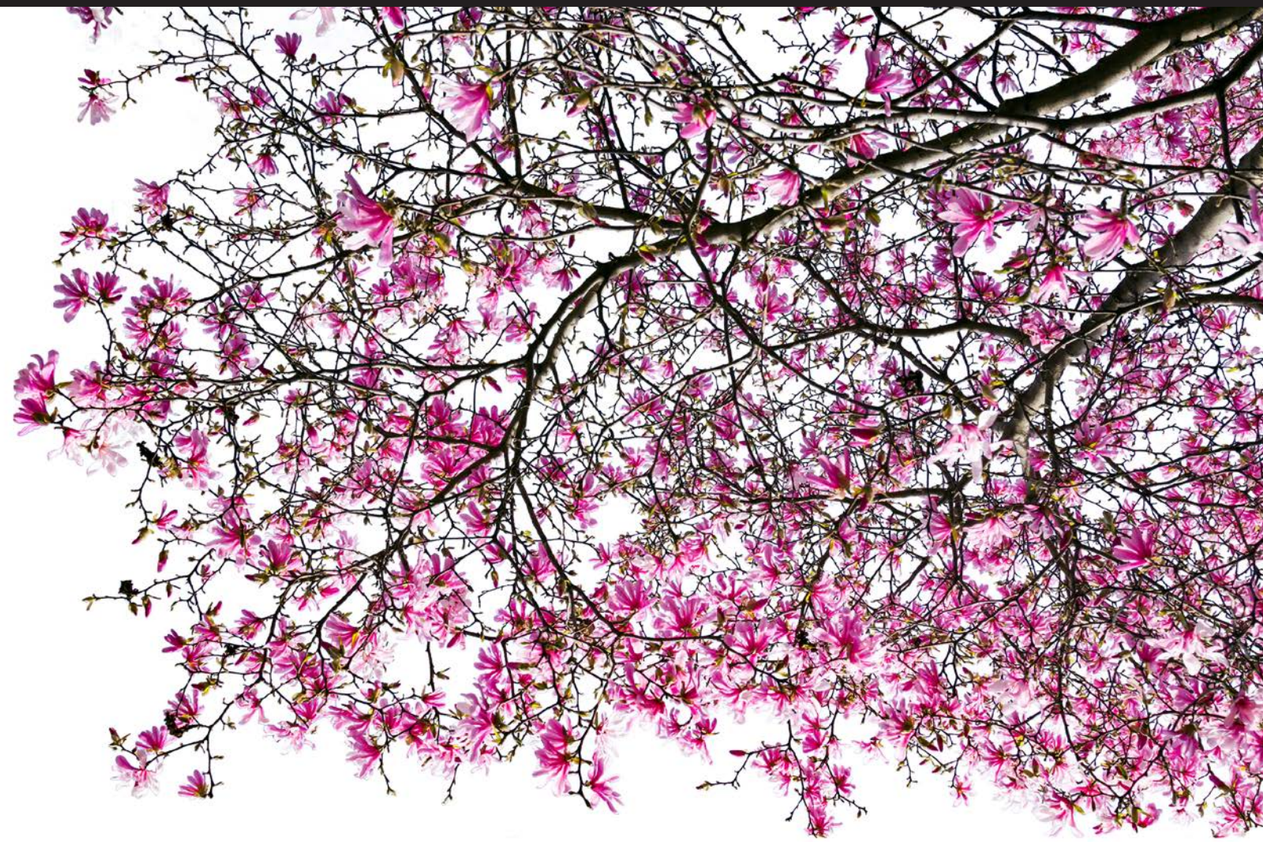
Sharma realized that these findings could help explain why advanced-grade and -stage cancers, including those that spread to the lymph nodes, are more prevalent in obese women with invasive breast cancer. So they set out to find a way to quiet leptin's hyperactive signaling in these tumors.

The Magnolia Medicine Cabinet

Magnolia's medical record is a long one, especially in places like China, Japan and the Korean peninsula. Records from China show that magnolia bark, called houpu, was used as early as 100 A.D. to treat digestion problems and breathing ailments, such as asthma. The bark, cones and leaves from a variety of *Magnolia* species are taken in their whole form, as extracts or powders, or most often brewed into an herbal tea. In traditional Asian medicine, magnolia is prescribed as an anti-inflammatory drug, an anti-anxiety medicine, a blood thinner and, yes—an anticancer agent.

The chemical compound called honokiol, extracted from magnolia seed cones, appears to be one of a handful of biologically active ingredients in the magnolia plant. Researchers have tested honokiol in cells grown in the lab and in animals, confirming that the compound does have an array of medicinal properties. In the 1990s, the Emory University lab of cancer specialist Jack Arbiser developed new ways to purify the compound, leading to a flurry of studies in his lab testing honokiol's anticancer properties against lymphocytic leukemia and myeloma, melanoma, breast and prostate cancers.

When Sharma and her colleagues began the search for a biologically active compound that would have anticancer activity and could shut down the leptin signaling network, honokiol leapt to the top of their list. It's a small molecule, which makes it easier for the body's cells to interact with and absorb. It doesn't appear to be toxic except in very high doses, and it isn't part of the hormone family that includes estrogen. This last point is important, says Sharma, because it means honokiol could "be used to treat estrogen receptor-positive as well as estrogen receptor-negative breast cancers."



How Honokiol Works

In two studies published last year in the journal *Oncotarget*, Sharma and her colleagues put honokiol under renewed scrutiny, first examining the effects of the compound on breast cancer cells grown in the lab. They discovered that honokiol can block the transformation and activation of some of the key molecules within leptin's signaling network in these cells—most notably, a signaling pathway that includes some well-known cancer-related proteins.

The researchers uncovered an especially intriguing role for a microRNA regulator called miR-34a. MicroRNAs are tiny snippets of genetic material that help to regulate how certain protein-coding genes are turned on and off. In a handful of other studies of miR-34a, scientists have identified the microRNA as an important tumor suppressor that is weakened in aggressive breast tumors. Now, for the first time, the Kimmel Cancer Center research team has shown that honokiol helps to keep miR-34a active and able to suppress some of the other cancer-linked proteins in the leptin network.

Sharma and her colleagues then fed some mice a high-fat diet and watched their leptin levels rise, compared to those in mice on a normal diet. Breast tumors grown in the obese, hyper-leptin mice had low levels of the protective miR-34a, they soon discovered, but these levels rose when the mice were fed doses of honokiol. Over four weeks of treatment, these tumors grew to be significantly smaller in obese mice treated with honokiol, to about the half the size of the tumors in untreated obese mice.

The link among obesity, leptin and breast cancer has been strengthened by these and other studies. But Sharma says the findings haven't yet changed how breast cancer patients are diagnosed or treated. "Currently, clinicians do not distinguish between leptin-induced or noninduced breast cancers," she explains. "It's not the usual clinical practice to check a patient for leptin or leptin receptor levels." She thinks the data collected by her lab and others will alter this practice in the future, especially since leptin signaling could affect how well standard breast cancer therapies work. Some studies suggest, for instance, that breast cancer cells that have been exposed to high levels of leptin over several years might be less sensitive to treatments like tamoxifen.

The next steps would be to begin a clinical trial of honokiol in breast cancer patients who are obese, "and then move toward tests of all patients who have this high-leptin state," Sharma says. ■

Construction Underway on Skip Viragh Outpatient Cancer Building: The 10th floor of the new building, scheduled to open in late 2017, will be home to the Under Armour Breast Health Innovation Center, including breast-specific treatment rooms, a gym, nipple tattoo area and a café.

Top: building rendering. Bottom, from left, Daniel Laheru and Elizabeth Jaffee, co-directors of the Skip Viragh Center for Pancreatic Cancer Clinical Research and Patient Care; William Nelson, Kimmel Cancer Center director; and Vered Stearns, director of the Breast Cancer Program, review blueprints of the new building.

Professor Lillie Shockney: Lillie Shockney, administrative director of the Breast Center, was promoted to professor of surgery. Shockney is the first nurse at Johns Hopkins to earn this appointment.

Knowing Your Breast Cancer Risk: On Nov. 8, 2015, our team held an educational symposium titled "Being Jewish and Breast Cancer Risk: What You Need to Know Now." It was presented by Judy Garber, director of the Center for Cancer Genetics and Prevention at Dana-Farber Cancer Institute. A medical oncologist, genetics counselor, epidemiologist and surgeon from community hospitals; a carrier of the BRCA breast cancer-related gene mutation; and a breast cancer survivor also participated. This program was supported by the Harry and Betty Lichtman Charitable Gift Fund.

Race for the Cure: Breast Cancer Program members were there for the 2016 Susan G. Komen Race for the Cure, staffing an educational table in Race Village for survivors, caregivers and families.

From left, Cindy Morin, Beth Thompson, Jill Mull, Antonio Wolff and Elissa Bantug, from the Kimmel Cancer Center, and Kelly Kesler and Mark Roeder from the Komen Foundation.

Cooking for Success: Just in time for Thanksgiving, author, educator and culinary expert Rebecca Katz hosted lunch and a healthy cooking workshop for patients and caregivers, instructing them on how to prepare foods that combat side effects. Participants received a signed, autographed copy of Katz's book.

From left, Christine St. Ours, Vered Stearns, Crystal Graham, Rebecca Katz, Jill Mull, Beth Thompson and Elissa Bantug

Survivorship Day: The second annual Breast Cancer Survivorship Day was held on May 21. More than 200 patients, children and caregivers attended the event, which included educational programming, speakers, panel presentations and breakout sessions. Ann Partridge, director of adult cancer survivorship at Dana-Farber Cancer Institute, delivered the keynote address. Children were entertained by Johns Hopkins medical, nursing and public health students with mad science, cupcake decorating, gymnastics, Lego building and circus performers. The event was funded, in part, by the Kimmel Cancer Center Breast Cancer Program, the Jane Rice Survivorship Program in Breast Cancer, Under Armour, Susan G. Komen Maryland and Genentech. The 2017 Survivorship Day is scheduled for April 1 at the BWI Marriott. For more information, contact Elissa Bantug at ebantug1@jhmi.edu.

Hitting It Out of the Park: More than 75 young breast cancer survivors and their guests enjoyed an afternoon of Orioles baseball as part of the Co-Survivors at Camden Yards event on July 24. Attendees were treated to a baseball game, lunch and a presentation on intimacy and breast cancer from social worker Sage Bolte.

Climb for Cindy Supporters Make a Difference

Chip Rosencrans has faced many figurative mountains since losing his wife, Cindy, to triple-negative breast cancer in 2009. This year, he took on a literal mountain to honor his wife's memory and raised $35,000 for breast cancer research at the Kimmel Cancer Center.

This summer, he climbed Mount Whitney in California. At 14,505 feet, it is the tallest mountain in the contiguous U.S.

"We set out from the Whitney Portal trailhead at a 7,851 foot elevation at 12:05 a.m. on Aug. 1 using headlamps to see the trail. By 5:30 a.m., sunrise showed the way and added some warmth," says Rosencrans. "Then, 9.5 hours from our start, at 9:30 a.m., we reached the summit at 14,505 feet, an elevation gain of 6,654 feet over 10.6 miles. We spent an amazing 1.25 hours at the summit, where I signed the logbook at the Smithsonian Hut (built in 1909) with the notation: 'Climb for Cindy.' Then, we began the descent, and by 5:30 p.m., we had made it back to the trailhead where we started the climb. The total hike was 21.2 miles over 17.5 hours."

"I am grateful to everyone who made contributions," says Rosencrans. "Research makes a difference." ■

Chip Rosencrans

Innovation Through Collaboration

UNDER ARMOUR CONTINUES to partner with Johns Hopkins scientists and clinicians in a joint mission to support innovative ways to empower breast cancer patients through risk assessment, prevention and treatment strategies, and overall well-being.

A new $1 million contribution supports unique research and patient care initiatives that shift the paradigm and bring positive change to women's health.

Five new grants will soon be awarded. The current Innovation Grants recipients are:

Nicholas Durr, Ph.D., Biomedical Engineering: A novel cryotherapy system for cost-effective breast cancer treatment

Josh Lauring, M.D., Ph.D., Oncology: Engineered hypermutated personalized breast cancer vaccines

Stuart Russell, M.D., Cardiology: Predictive Role of Baseline Physical Activity, Fitness, and Body Compositions in Patients Undergoing Breast Cancer Therapy and the Impact of Exercise on these Factors

Saraswati Sukumar, Ph.D., Oncology: A Grand Strategy to Accurately Diagnose and Treat Breast Cancer in Low and Middle-Income Countries

Tracy Vannorsdall, Ph.D., Psychiatry and Behavioral Sciences: Reducing Cancer-Related Fatigue and Improving Cognition with Transcranial Direct Current Stimulation

New Komen Grants Support Breast Cancer Tissue Bank and a New Radiation Therapy

Susan G. Komen announced new research grants totaling $512,500 for Johns Hopkins breast cancer investigators:

Komen Scholar **Antonio Wolff** will receive $62,500 to continue to build a repository of high-quality breast cancer tissue and blood samples that are linked to clinical data. This work could improve understanding of cancer development, help improve diagnostic tests and support studies testing new treatment options.

Jessie Nedrow will receive $450,000 to develop a new radiation-based targeted therapy that will only attack HER2-positive breast cancer cells, avoiding normal cells and tissues. Focusing on a targeted therapy that uses radiation should be more successful at treating primary and metastatic HER2-positive breast cancer cells since there is little chance of developing resistance using this approach.

Contribution Makes Important Immune Therapy Trial Possible

Immunotherapy has become a significant game changer in the treatment of some of the most difficult cancers. Antibody treatments that block the molecular immune checkpoints that prevent the immune system from fighting the cancer have resulted in impressive tumor shrinkage and long-term survival in melanoma, kidney and lung cancer patients.

Most of the groundbreaking work that led to these innovative treatments emerged from the laboratories and clinics of the Johns Hopkins Kimmel Cancer Center. Advances include three checkpoint-inhibiting drugs that are already FDA-approved for the treatment of advanced melanoma and lung cancer.

Based on these promising findings, a study in patients with advanced HER2-negative breast cancer, including triple-negative breast cancer, is planned. Studies in melanoma have indicated that when epigenetic and checkpoint blockade drugs are used in combination, the overall response rate is much higher—up to 60 percent better than with a single drug. "Our hope is that by utilizing this multidrug treatment regimen in breast cancer, we will be able to realize a response rate close to that seen in melanoma and the combination of epigenetic therapy with two immune checkpoint blockade drugs led to eradication of tumors and long-term cure in the majority of animals.

"OUR COLLEAGUES HAVE ALREADY DEMONSTRATED THAT RESEARCH FUNDING RESULTS IN IMPROVED IMMUNOTHERAPY APPROACHES IN ADVANCED, METASTATIC CANCERS. WE BELIEVE THAT OUR TEAM CAN ACCOMPLISH THE SAME FOR BREAST CANCER." **–VERED STEARNS**

With a pledged gift for up to $500,000 from the Lefkofsky Family Foundation, we now have the opportunity to explore their promise in breast cancer. Although studies of immune checkpoint therapies in patients with metastatic triple-negative breast cancer—one of thae most treatment-resistant forms of breast cancer—were promising, the results do not yet mirror the exceptional outcomes seen in melanoma. Most triple-negative breast cancer does not seem to naturally attract the attention of the immune system, so strategies to improve the response to immune checkpoint agents are greatly needed.

We already know that the epigenetic changes (changes to the chemical environment of DNA) occur at the sites where genes are switched on or off and can lead to cancer development and growth. New drugs that specifically target these epigenetic alterations represent an active and promising field of investigation in cancer therapeutics. Combining drugs that target epigenetic alterations with immune checkpoint blockade may convert breast tumors that currently do not respond to immunotherapy to breast tumors that do respond. In animal breast cancer models, at least double what is currently seen with single-agent therapies," says Vered Stearns, director of the Kimmel Cancer Center's Breast and Ovarian Cancer Program. "The response rate to standard chemotherapy in triple-negative breast cancer is currently quite low, so we are hopeful that this approach will convert advanced breast cancer into a more treatable, and ultimately curable, disease and provide a new and effective option for our patients and their families."

"Our colleagues have already demonstrated that research funding results in improved immunotherapy approaches in advanced, metastatic cancers," says Stearns. "We believe that our team can accomplish the same for breast cancer, and we are grateful to the Lefkofsky Family Foundation for helping us make it happen and for their support over the years."

In addition to this project, the Lefkofsky Family Foundation supported two pancreatic cancer studies—one for the development of a novel monoclonal antibody for detection and treatment and a prevention study utilizing Elizabeth Jaffee's pioneering pancreatic cancer vaccine. ■

Realizing the Promise of Breast Cancer Prevention

THE JOHN FETTING FUND

"I support the Fetting Fund so that future generations may never have to experience breast cancer. The risk is elevated for my kids and their own children because I am a metastatic breast cancer patient. The Fetting Fund may find preventive measures and treatment to help people at greater risk, and that is such an important mission." –BRENDA CHO

The John Fetting Fund for Breast Cancer Prevention supports the most promising research in breast cancer prevention. By improving our understanding of who is at most at risk for breast cancer, we can focus our efforts on those individuals and come up with better ways to screen women and reduce their risk. Prevention research also helps us identify those who are at lower risk and may not need aggressive screenings and prevention techniques.

CONNECT WITH US:
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JOHNS HOPKINS
BREAST MATTERS
A publication of the Sidney Kimmel Comprehensive Cancer Center
at Johns Hopkins Office of Public Affairs

Help Us Make A Difference

Each contribution to the Breast Cancer Program at the Johns Hopkins Kimmel Cancer Center makes a difference in the lives of cancer patients here at Johns Hopkins and around the world.

Our physician-scientists are leading the way on many of the scientific breakthroughs in breast cancer, and your donation will support patient care and innovative research that is translated to better, more effective treatments. We are also focusing on ways to prevent breast cancer and support survivors.

You may designate a gift to a specific faculty member.

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Baltimore, MD 21202

To contact our Development Office by phone, fax or email:
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Fax 410-230-4262
Email: KimmelGiving@jhmi.edu

Visit us on the Web at **hopkinscancer.org.**
Click on Breast Cancer Program, left column.

If you prefer not to receive fundraising communications from the Fund for Johns Hopkins Medicine, please contact us at 1-877-600-7783 or JHHOptOut@jhmi.edu. Please include your name and address so that we may honor your request.

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The John Fetting Fund for Breast Cancer Prevention
funding the most promising research in breast cancer prevention

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Learn more at http://bit.ly/fettingfund

Exercise and Cancer: Dec. 6, 7–8 p.m.
Events are free to participate and open to all patients, caregiver, providers and community members, but pre-registration is required.
http://bit.ly/JHUCancerSurvivorshipWebinars

JOHNS HOPKINS MEDICINE