

THE JOHNS HOPKINS KIMMEL CANCER CENTER

BREAST MATTERS



**How Integrative Medicine is
Helping Breast Cancer Patients**

2021/2022

BREAST MATTERS

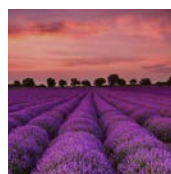
THE NEWSMAGAZINE OF THE BREAST CANCER PROGRAM **2021-2022**

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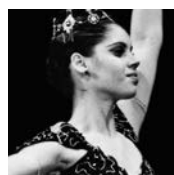
Blood Tests That Detect Breast Cancer

Help Guide Treatment by Identifying Cancer Recurrences



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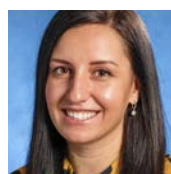
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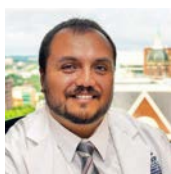
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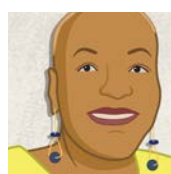
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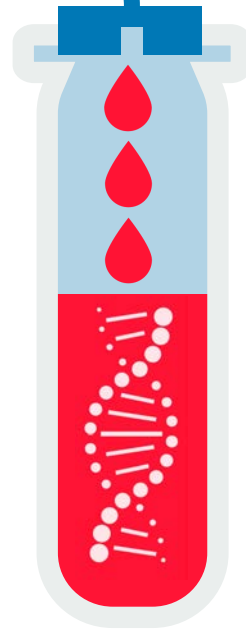


SAGE Strong

A Holistic and Individualized Approach for Women Living with Breast Cancer

[Liquid Biopsies]

BLOOD TESTS THAT DETECT BREAST CANCER



Jill Phallen



Jessica Tao



Emily Ambinder

For scientist **Jill Phallen, Ph.D.**, early detection provides the best opportunity to help the most people. She is working with medical oncologist **Jessica Tao, M.D.**, and radiologist **Emily Ambinder, M.D., M.S.**, to develop liquid biopsies — tests that identify genetic mutations specific to cancer in blood and body fluids — to improve early detection of breast cancer, monitor for a cancer’s return and guide treatment decisions.

“For breast cancer, there is a screening paradigm,” says Dr. Phallen. “Mammography works very well, but there is a subset of patients who have a predisposition to breast cancer and other cancers.” Those with mutations to BRCA1 or 2 genes have a 55% or

more chance of developing breast cancer by age 70, she says.

BRCA stands for breast cancer susceptibility genes, and a mutation in BRCA1 or BRCA2 alters the body’s ability to repair DNA, leading to the increased risk of developing breast cancer.

This risk puts many women in an unthinkable position, with some opting for mastectomies and salpingo-oophorectomies — removal of the fallopian tubes and ovaries — to prevent cancer.

Drs. Phallen, Tao, Ambinder and colleagues want better options for patients and those at risk.

“We thought this would be a good opportunity to apply liquid biopsy approaches,” says Dr. Phallen, referring

BRCA (Breast Cancer Susceptibility) genes alter the body’s ability to repair DNA, leading to the increased risk of developing breast cancer. Liquid biopsies — tests that identify genetic mutations specific to cancer in blood and body fluids — help improve early detection of breast cancer and guide treatment decisions and therapies.

to techniques that find evidence of cancer-related DNA shed into the bloodstream. She and her colleagues hope the approach can complement mammography and better inform mammogram results.

Mammograms can often have suspicious results that cause stress and worry to the patient and may lead to unnecessary interventions, Dr. Tao explains. Liquid biopsies might help doctors verify concerning results.

A new approach developed in the laboratory of cancer genetics expert **Victor Velculescu, M.D., Ph.D.**, is one of the liquid biopsy tests being studied. It’s called DELFI, for DNA evaluation of fragments for early interception. It spots unique patterns in DNA shed from cancer cells circulating in the bloodstream.

Healthy cells package DNA like a well-organized suitcase, but cancer cells are more like disorganized suitcases with items from across the genome thrown in haphazardly, Dr. Velculescu explains. DELFI detects this telltale sign of cancer, which



From left, top row: Victor Velculescu, Vered Stearns, Nadine Wilder, Jenna Canzoniero, Jennifer Lehman, Kavya Boyapati; bottom row: Kala Visvanathan, Rob Scharpf, Jill Phallen, Emily Ambinder, Jessica Tao, Morgan Buckley.



Victor Velculescu Vered Stearns Kala Visvanathan

occurs across all cancer types, providing an opportunity to detect cancers early.

Dr. Phallen is working with Drs. Velculescu, Ambinder and Tao, biostatistician **Rob Scharpf, Ph.D.**, breast cancer experts **Vered Stearns, M.D.**, and **Kala Visvanathan, M.D., M.H.S.**, and colleagues at the University of Pennsylvania to use data collected through mammography of 1,000 healthy women and women with breast cancer to improve the ability of DELFI to distinguish healthy cells from breast cancer cells. The study is supported in part by the Basser Initiative at the Gray Foundation and the John Fetting Fund for Breast Cancer Prevention. With additional funding, Dr. Phallen and colleagues

hope to expand the research to ovarian and other cancers.

Dr. Tao says liquid biopsies can help guide treatment by identifying cancer recurrences and finding gene alterations that are driving the cancer and could be targeted with drug therapies. Implementing liquid biopsies has the promise, she says, to detect cancers before they can be seen on imaging or cause symptoms.

Liquid biopsies have also been used in other cancer types and to guide treatment of more advanced breast cancer.

In studies of advanced cancers, including IMAGE (Individualized Molecular Analyses Guide Efforts in Breast Cancer), which compared cancer DNA detected in tissue samples with liquid biopsies, found that liquid biopsies were faster and as good as tissue samples for detecting tumor DNA. IMAGE2 expands the comparison of genetic profiling of tissue samples with liquid biopsy and compares liquid biopsies taken before and after treatment to look for changes in

cancer DNA. Patients participating in IMAGE2 have their tumor profiles discussed with the Johns Hopkins Kimmel Cancer Center Molecular Tumor Board, which helps identify targeted therapies for patients based on the unique genetic signatures of their tumors. The IMAGE studies are consistent with earlier efforts at the Kimmel Cancer Center showing non-invasive liquid biopsies can rapidly and accurately determine response to cancer treatments.

“Right now, we have to wait three months and do an imaging scan to see if a drug is working,” says Dr. Stearns. “We want to see if we can do a liquid biopsy after a week and tell if a therapy is working. If it’s not working, then we can quickly switch course. We would rather know sooner than later. We don’t want to lose three months.”

Liquid biopsies aren’t standard of care yet, Dr. Tao explains, but “our long-term vision is that years from now we will have this noninvasive way to screen patients for breast cancer.”



BALLERINA TURNED DOCTOR

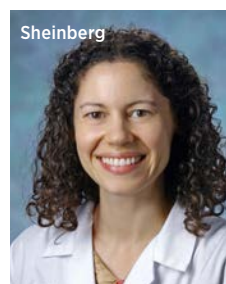
How She Is Using
Integrative Medicine
to Help Patients
with Breast Cancer

PERSONAL EXPERIENCES WITH pain and injury led **Rosanne Sheinberg, M.D.**, a ballerina turned anesthesiologist, to integrative medicine and a desire to help patients with breast cancer and other diseases improve their health and quality of life.

It's not as unusual of a transition as it sounds, she explains. "Most people think ballet and medicine are far apart, but that's not true," says Dr. Sheinberg. "Both fields require uber concentration and nose-to-the-grindstone work for many years."

In addition, she says, ballet dancers have a natural interest in the body. It's the tool of their trade, after all. Ballet

dancers have a high rate of injury from over-use of muscles and tendons, so doctors' visits, orthopaedic surgery and, unfortunately, aches



and pain, are common occurrences. This necessary interaction with health care providers leads many dancers to go into the health field, she says.

Dr. Sheinberg's journey from ballerina to doctor began when she was spotted by the Joffrey Ballet, one of the premier ballet companies in the U.S., during a high school dance competition. After graduation, instead of heading off to college, she left her home in California for New York City to join the prestigious ballet company.

Frequent injuries that were certain to limit the length of her career as a ballerina prompted her to pursue a career in medicine. An unfortunate interaction with a dismissive cruise ship physician, who refused to take seriously a shoulder injury that occurred during a dance performance on the ship, literally added insult to injury. It helped her cement in her mind what kind of doctor she would become.

"He rolled his eyes at me. He didn't believe I was injured," she recalls. "That stung. It felt lousy not to be believed, and I was ethically driven toward a career in medicine. I would never do this to someone."

She wanted to be the kind of doctor patients could turn to for emotional and physical care. "If patients tell us they are suffering, we have to believe them," she says.

Choosing Anesthesiology

In 2002, she started medical school at Johns Hopkins and chose anesthesiology as her specialty.

She describes anesthesiologists as the unsung heroes in medicine. Unlike her career as a ballerina taking center stage with all eyes on her, as an anesthesiologist she works behind the scenes.

The anesthesiologist is a somewhat anonymous figure who delivers anesthesia for surgery and regulates all the body's functions, from blood pressure to respiration, during the operation. They are a composite of physician and guardian angel, someone the patient can trust to care for them when they are most vulnerable.

Anesthesia, she says, is medicine in

fast forward, requiring the physician to have a plan ready and to act immediately if blood pressure drops or another complication occurs. If one drug doesn't work, she must try another. This experience, and in particular her specialty in cardiac anesthesia, made her see integrative medicine as the path to optimizing health for people with failing hearts.

Now, through a collaboration with **Vered Stearns, M.D.**, director of the Women's Malignancies Program, and **Karen Smith, M.D., M.P.H.**, a breast cancer and survivorship specialist, and with support from Under Armour, Dr. Sheinberg is helping breast cancer patients feel better and do better.



Quick Reference Guide to Integrative Medicine

A five-pronged approach to minimizing chronic inflammation to enhance survivorship



- **NUTRITION:** Avoid added sugars and processed foods. Choose whole foods, fruits and vegetables, and healthy proteins.

- **SLEEP:** Get outdoors. Sunlight in the morning aids sleep at night. Exercise is key. To get good sleep at night, the body needs to move during the day. If a restless mind is interfering with sleep, try imagery and calming music. If a restless body is the problem, toe tapping may help.

- **STRESS MANAGEMENT:** Learn your body's stress triggers. Respond to stress with slow, deep breathing to return to a calm state.

- **EXERCISE:** Those who sit most of the day, should stand for a few minutes every hour. Aim for strength or resistance training two to three times per week. For heart health, add fast walking, jogging or high intensity intervals for at least 30 minutes, three times per week.

- **CONNECTION:** Look to something more meaningful and larger than yourself through religion, nature, family or a combination of these to go from a mindset of fear and anxiety to one of gratitude and service.

Understanding Integrative Medicine

What is integrative medicine? Dr. Sheinberg explains it has two buckets, with changes in lifestyle as one component and an expanded toolkit that includes supplements, yoga, acupuncture and other complementary approaches that can be tried during and after treatments to mediate side effects.

She wants people to understand that physical illness and overall well-being are interconnected.

Experts have revealed so much in recent years about the genetic (mutations to our DNA) and epigenetic (chemical changes to our DNA) causes of cancer, but it's not the full picture, she says. Chronic low-grade inflammation brought on by stress impacts survivorship.

We are meant to exist in balance, she says, but the problem is that most people are living out of balance, stressing over health, jobs, money, kids — the list goes on and on. This kind of chronic stress causes the body to release hormones that are associated with worse health outcomes, particularly in people with cancer, she explains.

"The way we live our lives may cause the low-grade inflammation, but there are things we can do to be proactive and help patients help themselves," she says. "This should not be a shame and blame game. Instead, I want to give patients information and let them make choices, based on scientific evidence, to modify their lifestyles to feel better and live better."

Her overarching goal is help patients limit and minimize inflammation produced by the body. She uses a five-pronged approach aimed at improving nutrition, sleep, stress, exercise and a connection to something meaningful.

Dr. Sheinberg tries to keep it as simple as possible so patients do not feel overwhelmed or defeated.

Nutrition

Too often, she says, patients are encouraged by well-meaning family, friends and even health care providers sometimes to eat whatever they want. After all, they have been dealt a bad hand. They have cancer. Sometimes, high-caloric diets are encouraged to combat weight loss caused by cancer. Dr. Sheinberg says she wants patients to know they can fight back with healthy changes to diet.

She recommends an anti-inflammatory diet, and lets patients know that the two most inflammatory food choices are anything with added sugar and processed foods. She recommends being aware of ingredients when grocery shopping.

"If it has more than five ingredients on the list, and you don't understand what most of them are, stay away from it," she advises.

Go for a rainbow of colors, she suggests, choosing whole foods, fruits and vegetables — more vegetables than fruits — whole grains, legumes, healthy fats like olive oil, nuts, seeds, olives and avocados, and healthy proteins.

She recommends making meat the side dish instead of the main course. Modest amounts of soy in the diet are good, she says, dispelling a myth that patients with breast cancer should avoid soy because plant estrogens stimulate cancer.

Vegetables create a healthy gut microbiome with the right balance of bacteria and microbes, and that helps create a healthy immune system, she says. Yogurts with active cultures also help the gut. What often won't help, she says, is supplements.

"They can be a useful early step, but they are not a long-term fix. You can't overcome poor nutrition with supplements and probiotics," says Dr. Sheinberg. This is particularly important for patients during treatment. Some supplements can interact with

cancer treatment, so she recommends staying away from supplements and focusing on diet.

Sleep

For women with breast cancer, hot flashes can be a key disruptor of sleep. Dr. Sheinberg collaborates with gynecologist **Wen Shen, M.D.**, clinical director of the menopause consultation service and co-director of the Women's Wellness & Healthy Aging Program, to



get solutions for women suffering sleep loss due to hot flashes.

The recipe for a good night's sleep actually starts in the morning with sunshine, Dr. Sheinberg says. "If you don't get morning sunlight on your eyes, it interferes with the body's circadian rhythm," she says, referring to the natural internal process that regulates a person's daily sleep-wake cycle. People who stay indoors all day often have difficulty falling asleep at night, she says.

Dr. Sheinberg also helps patients determine if it's a restless mind or restless body that is interfering with sleep, adding that a restless mind is more common among those with cancer. For patients whose mind is racing with thoughts as they try to settle in for sleep, Dr. Sheinberg teaches guided imagery techniques, which involves focusing the imagination on things the patient finds peaceful, such as a favorite place. Calming music is another technique.

For those suffering from a restless body, toe tapping is among the techniques that may provide relief. Dr. Sheinberg adds this is another area where exercise is important. "Our body needs to move. A person cannot settle in for sleep if they have not moved throughout the day," she says.

"If it has more than five ingredients on the list, and you don't understand what most of them are, stay away from it."

Stress

Dr. Sheinberg spends at least 90 minutes with new patients. She wants to really get to know the patient, to see if there are learned lifelong patterns that have become the body's trigger to initiate a stress response. Then, once patients understand their triggers, she teaches them how to respond to stress with slow deep breathing, movement therapy and other skills. Once they learn how to use these techniques to calm themselves, they can employ them as needed to de-stress.

Some situations call for more involved interventions. Dr. Sheinberg recalls an elderly patient who lived alone and was feeling isolated during the height of the COVID-19 pandemic in 2020. She expressed to Dr. Sheinberg that, for the first time in her life, she was feeling depressed. Dr. Sheinberg suggested massage therapy as a way for her to safely experience a personal connection. It worked. The patient cried tears of joy as she described feeling nurtured again.

Exercise

"Sitting is the new smoking," says Dr. Sheinberg, referring to a statement coined by endocrinologist Dr. James Levine related to the harmful health effects of sitting all day long, whether it's at a desk, in a car or on a sofa at home. Dr. Sheinberg recommends that patients who spend most of their day sitting pop up every hour for a minute or two.

Exercise is the best way to combat cancer-related fatigue, Dr. Sheinberg says. It also provides a physical boost to help the body resist toxic side effects of therapy, she says.

For patients in active treatment, Dr. Sheinberg recommends gentle exercise, such as yoga. She helps patients in treatment with individualized exercises.

Strength or resistance training with

weights or body weight is critical to preventing bone loss and preserving muscle mass, and is recommended two to three times per week.

"The best thing a person can do to improve chronic arthritis pain is strength training," she says. "There is nothing better. It often works better than drugs."

Additional cardiovascular exercise is also recommended, with a goal of at least 30 minutes, three days per week.

Adding fast walking, jogging or high-intensity intervals to a daily walk is a heart-healthy exercise, she says.

Connection

Dr. Sheinberg guides patients to look to something more meaningful and larger than themselves. It could be religion, nature, family or a combination of these, she says.

"This can be a huge switching point," says Dr. Sheinberg. "When patients go from a mindset of fear and anxiety to one of gratitude and service, suffering plummets."

Our bodies respond to our mindset. Expressing gratitude in thought and action, she says, supports positive chemical changes in our bodies. Conversely, when a person is fearful or anxious, the body's fight or flight responses kick in, leading to responses from our adrenal glands and inflammatory cells called cytokines. She teaches mental exercises to help patients shift the focus of thoughts to something positive. When they begin feeling anxious or fearful, they can train their bodies to interrupt this process.

In her five-pronged approach, Dr. Sheinberg tailors recommended techniques and interventions to the individual needs of each patient.

"It has to work for the patient, or it is useless," she says. "Each patient is unique. We have to appreciate that to understand their needs."

"When patients go from a mindset of fear and anxiety to one of gratitude and service, suffering plummets."

Brunetta's Story

Brunetta, 64, was already feeling stress related to the health issues of family members when she was diagnosed with early stage cancer. She was anxious as she awaited her surgery, still several months off, when she was referred to Dr. Sheinberg.

"I started feeling like I needed the surgery to hurry up and happen. Dr. Sheinberg helped me understand that I could heal my train of thought," she says. "I felt like I was back on course after one visit. We talked for over an hour. She helped me so much."

Brunetta learned breathing and imaging techniques that helped her stay calm. When she feels stress creeping in, she uses these techniques and prayer to get back to "that place of calm." Brunetta describes it as going into a space where her mind takes her to a place of peacefulness.

Thank You, Under Armour!

Thank you to Under Armour and the generous donation that established the Under Armour Breast Health Innovation Center, which bolsters the patient



experience. Through ongoing support, other providers have been integrated

into our practice, including physicians from physical medicine and rehabilitation and integrative medicine. Dr. Rosanne Sheinberg, the Director of Integrative Medicine for Anesthesiology and Critical Care Medicine, expanded her acupuncture practice to include cancer outpatients. With Under Armour support, Dr. Sheinberg sees breast cancer patients twice monthly in the Skip Viragh Outpatient Cancer Building for new and follow-up appointments. This new service added 45 new patients, and counting.

“She really helped me get a grip on overthinking,” says Brunetta.

She focused on eating better, including more fruits and vegetables in her diet, eliminating sugar and switching to healthier proteins, including chicken, fish and tofu. Brunetta says she lost weight and feels better.

A religious connection was key for Brunetta.

“God is helping me handle this. That’s what keeps me going. When fear comes back, I connect and come away from it,” she says. “I am going to recover and move on with my life, and Dr. Sheinberg helped me understand that part of recovery is taking care of myself. I know I’m moving in the right direction.”

Azadeh’s Story

For Azadeh, the path to recovery has been more challenging. Tissue expanders placed in her breast to prepare her body for future breast reconstruction caused her great discomfort and sometimes made it difficult to breathe.

Azadeh had been through two surgeries and says she was feeling desperate when her oncologist, Dr. Vered Stearns, referred her to Dr. Sheinberg, who spent two hours talking with her. She wanted to fully understand Azadeh’s medical history and the extent of her current issues.

“It was extremely reassuring that she would take that much time to understand what was wrong with me so she could make recommendations,” says Azadeh.

Although having the expanders removed relieved Azadeh’s most serious symptoms, she was still in pain. She was excited that Dr. Sheinberg offered drug-free approaches, including physical therapy, yoga treatment, nutritional changes to reduce inflammation, acupuncture, electrical stimulation to the area of pain, and myofascial release therapy, which helps relax contracted muscles.

Azadeh says she is experiencing gradual progress with the yoga, physical therapy and myofascial release

therapy. She appreciates that Dr. Sheinberg continues to offer additional non-pharmaceutical solutions aimed at further improvement of her symptoms.

“The passion and compassion for the patient she brings to her practice is something I have rarely seen,” says Azadeh.

Anne’s Story

Anne’s situation was different still. She turned to Dr. Sheinberg after her breast cancer diagnosis two days after her 70th birthday left her feeling exhausted. She wanted to learn ways to boost her energy and to find remedies for numbness in her toes caused by treatment-related neuropathy — damage to the nerves in her feet — and problems with shoulder mobility.

Anne had always focused on leading a healthy life. “My only risks were aging and being a woman,” she says. “I was really ready, after months of tests and treatment, to learn and implement how to up my game, knowing now for certain that preventing future cancer was definitely at stake.”

She describes herself as feeling defeated when she first met with Dr. Sheinberg. She was fighting fatigue and lethargy, just coming off six months of cancer treatment.

“I hadn’t realized that life after the discovery of cancer and treatments would be so exhausting, difficult and confusing, and how depleted I’d feel,” says Anne. “Recovery and dealing with persistent or new side effects was so demanding and time-consuming.”

Dr. Sheinberg recommended Anne try qi gong — mind-body exercises focused on meditation, breathing and movement — to regain strength and energy.

“She confirmed my lifelong awareness of healthy living practices, many of which had fallen by the wayside as life happened,” says Anne, who lives on the Eastern Shore of Maryland and was able to meet with Dr. Sheinberg through telemedicine visits — video conferences through Johns Hopkins’ secure web portal.

When acupuncture did not relieve Anne’s neuropathy, Dr. Sheinberg recommended exercises that might stimulate the nerves.

“Now, I have physical therapy stations throughout my house,” says Anne.

She says Dr. Sheinberg explained the importance and ways of reducing inflammation in the body.

Anne made changes to her diet, like eating fewer sweets, including less chocolate, one of her favorite treats and substituting green tea in place of an afternoon coffee.

“Dr. Sheinberg is an ally. I am so grateful to her. She is full of information and provides up-to-date, clinically sound recommendations, backed by research,” says Anne.

“I ask 1,000 questions, and she has 1,000 answers.”

Anne says she is making great strides and looking forward to returning to horseback riding and archery.

“Working with integrative medicine and Dr. Sheinberg is like having an enthusiastic coach, Anne says. “Integrative medicine supports—in practical and less tangible ways—the importance of reclaiming joy in life, empowerment, engagement in one’s own healing and in resuming normal life.”

When she was diagnosed with cancer, her mind was set on coming to Johns Hopkins for care because of its stellar reputation, and she says her experience met her high expectations.

“I felt lucky to have Dr. Sheinberg as part of my care team. She’s absolutely as vital a part of my Hopkins team as my three wonderful oncologists,” says Anne. “Integrative medicine is as important a part of the treatment and healing process as conventional medical, surgical and radiation therapies. I was grateful to be at a place that offered this kind of care.”



UPDATED SERVICES

BREAST CANCER SERVICES ARE EXPANDING AT THE KIMMEL CANCER CENTER AT GREEN SPRING STATION.

Patients with breast cancer can now receive all of their care at Green Spring Station, says **Rima Couzi, M.B.B.Ch., M.H.S.**, a medical oncologist practicing full time at this location.

The surgery program continues to grow since the opening of Pavilion III in 2019. Four surgeons, **Melissa Camp, M.D., M.P.H.**, **Julie Lange, M.D.**, **David Euhus, M.D.**, and **Mehran Habibi, M.D.** --now see patients with breast cancer at our Green Spring Station locations. A new surgical suite is open on the third floor of Pavilion III for lumpectomy and other surgeries.

Medical oncology services are also expanding, and the number of

clinical trials available to patients is growing. In addition to Dr. Couzi, **Deborah Armstrong, M.D.**, **John Fetting, M.D.**, **Danijela Jelovac, M.D.**, **Jennifer Sheng, M.D.**, and **Antonio Wolff, M.D.**, also see patients at the Green Spring Station location from one to four days per week.

Radiation oncologist **Fariba Asrari, M.D.**, also sees patients at Green Spring Station.

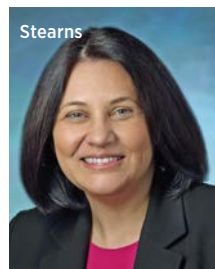
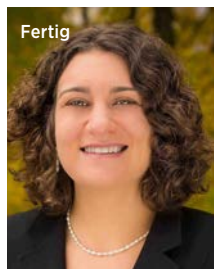
The multispecialty team includes **Eden Stotsky-Himelfarb, B.S.N., R.N.**, who joined the breast cancer program as a nurse coordinator to help guide patients through their care. When needed, patient navigator **Jill Mull, M.Ed.**, works with

patients who have breast cancer of all stages and survivors of all ages. She also has a particular focus on young women with breast cancer and their families.

One additional perk for patients is the recent opening of a beautiful new healing garden outside of Pavilion III.

“The facilities are new and comprehensive, with surgery, medical oncology, radiation oncology, and imaging services on site,” says Dr. Couzi. “Our ultimate goal is to make it easier for people live locally and in northern Pennsylvania to get all of their services at our Green Spring Station location.”

IMMUNOTHERAPY NEWS



Developing Immunotherapy for Estrogen Receptor Positive Breast Cancer

A new clinical study is aimed at developing immunotherapies before surgery (preoperative or neoadjuvant) for early-stage estrogen-receptor positive (ER+) breast cancer, the most common subtype of breast cancer.

"This is a huge population of patients," says breast cancer expert **Cesar Santa-Maria M.D., M.S.C.I.**, who is leading the study. Some patients do well with treatments that block the hormone estrogen, but others do not, he says, so he is working to find new treatment options for these patients.

He is collaborating with **Vered Stearns, M.D.**, Director of the Women's Malignancies Program, **Elizabeth Jaffee, M.D.**, Director of the Convergence Institute and Associate Director of the Bloomberg-Kimmel Institute for Cancer Immunotherapy, and **Elana Fertig, Ph.D.**, Co-Director of the Convergence Institute and Director of Quantitative Sciences.

Working together, they are learning how the tumor microenvironment--the nest of immune cells, blood vessels, proteins and more in which a cancer lives--is altered by the cancer to maintain its survival.

"As we begin to understand this at a deeper level, we are hopeful it will shed light on how to develop better immunotherapy combinations," says Dr. Santa-Maria.

In this study, the researchers are evaluating a combination of the drug nivolumab, which promotes an im-

mune response to cancer, with an anti-hormone drug for patients with early stage ER+ breast cancer. Half of the patients will also receive a CDK4/6 inhibitor--a targeted therapy that interrupts the ability of breast cancer cells to divide and multiply, and may also cause changes to cancer cells that make them more visible to the immune system.

The study, which is supported by the National Cancer Institute, Pfizer and Allegheny Health Network grants and a Passano Foundation award, is open at the Kimmel Cancer Center, including the Sibley Memorial Hospital location, the Allegheny Health Network and University of Alabama. More information is available at clinicaltrials.gov (search for NCT03573648).

PRISMM Study A Virtual Clinical Trial for Patients with Metastatic Cancer and Spliceosome Mutations

The PRISMM (Patient Response to Immunotherapy using Spliceosome Mutational Markers) study has a unique virtual design open to patients with advanced breast cancer who are being treated anywhere in the mainland U.S. It will soon be available to patients with any type of metastatic cancer. The study's focus is on RNA editing cellular

machinery that influences protein production, called the spliceosome. Rare spliceosome mutations cause variations in protein production that make cancer look unusual enough to the immune system to draw a response.

The study explores whether using immunotherapy to treat patients with these rare mutations (specifically SF3B1, U2AF1 or SRSF2) can incite their immune systems to attack their cancers. Most commercially available genetic testing of tumors, such as those by Foundation Medicine, CARIS, and TEMPUS, evaluate spliceosome mutations. If patients or their doctors think that they may have a qualifying spliceosome mutation (SF3B1, U2AF1 or SRSF2), the patient can log on to bit.ly/3PRISMM and enter some basic information and upload their genetic testing report. Patients confirmed to have spliceosome mutations will be evaluated by our Molecular Tumor Board, and recommendations for immunotherapy drugs that might work against the cancer will be provided to patients and their oncologists. Treatment is handled by the patient's local oncologist, but the PRISMM study team remains in contact with questionnaires.

"It's a new way to think about clinical trials and increasing access to clinical trials to patients around the country," says Dr. Santa-Maria. With the ongoing COVID pandemic, the ability to participate remotely is an added bonus for patients.

To learn more or to enroll in the study, visit the clinical trial website at bit.ly/3PRISMM, or go to clinicaltrials.gov (search for NCT04447651).

DONOR SPOTLIGHT

We Can't Do This Without You!

Thank you to the many generous donors who support the Kimmel Cancer Center researchers and clinicians working to better understand and improve treatments for metastatic breast cancer, including Twisted Pink and Hope Scarves.

HIGH IMPACT PHILANTHROPY

Judith A. Lese Breast Cancer Foundation

Judith Lese — 74, mom of three, retired teacher, and breast cancer survivor — is



helping extend the promise of immunotherapy to breast cancer patients. The Judith A. Lese Breast Cancer Foundation, which she established in 2003 as she was waging her own personal battle against breast cancer, has supported immunotherapy research at the Kimmel Cancer Center for nearly two decades.

Breast cancer is the second-leading cause of cancer-related death in women, and new treatments are urgently needed, says Vered Stearns, M.D., Director of the Women's Malignancies Program. Immunotherapy has been a game changer in some tumor types, but has perhaps been less effective in breast cancer. Dr. Stearns and Dr. Cesar Santa-Maria, breast cancer immunotherapy expert, believe breast cancer may create an environment in the tumor that prevents the immune

system from eliminating tumor cells, called an immunosuppressive tumor microenvironment. Novel immunotherapies harness the body's immune system to fight cancer, holding great promise to prevent tumor recurrence and prolong survival. Dr. Santa-Maria and others are studying new strategies to decrease these suppressive signals in the tumor and replace them with antitumor signals to successfully eliminate tumor growth. They are also investigating differences in the immune response to early-stage breast tumors compared with breast tumors that have spread or metastasized to areas outside the breast.

"I feel like I benefited from research and excellent care," says Ms. Lese, who received her cancer treatment at the Johns Hopkins Sibley Memorial Hospital in Washington, D.C. "As long as I'm alive, my mission is to do whatever I can to help save the lives."

NEW DEVELOPMENTS

GENETIC TESTING

DRUG RESISTANCE

HIGH-RISK SCREENING



A targeted drug therapy, called PARP inhibitors--which prevent damaged cancers cells from repairing themselves--are moving from the treatment of advanced breast cancers to treatment of early-stage breast cancers, particularly for patients whose cancers have BRCA1 or BRCA2 mutations.

New study results suggest that women with early breast cancer at high-risk for recurrence who carry the BRCA1 or 2 gene and completed recommended local therapy (surgery, radiation) and chemotherapy may be candidates for treatment with a PARP inhibitor for one year.

“This is a major clinical advancement and another important reason for patients to think about genetic testing,” says John Fetting Fund for Breast Cancer Prevention scholar **Kala Visvanathan, M.D., M.H.S.** “There is now a panel of genes we look for in breast cancer, to help tailor early detection and preventive care and in some cases treatment options. We need to increase awareness, uptake of genetic testing and appropriate follow up,” Dr. Visvanathan says. “As new discoveries occur we want all individuals to have access to them

and the opportunity to benefit from them.”

One of Dr. Visvanathan’s goals is to ensure that minority groups and underserved populations understand the value and have access to genetic testing. She and her colleagues, including communication expert Dr. **Katherine Smith**, are working on designing short patient-driven culturally sensitive videos to help patients and their family members understand the reasons and importance for considering genetic testing. The hope is that it will encourage more genetic testing among patients and relatives who

have strong family histories of breast and other cancers.

The first of these studies is called PREVIEW for patient review and personal feedback on personal experiences about cancer genetics for African Americans. It is supported by the WellSpan-Johns Hopkins Fund.

Dr. Visvanathan is also using novel technology, such as artificial intelligence, to improve patient access to high quality genetic education and appropriate referral to our genetics experts when needed. A study called Evaluation of Novel Approach to Genetic Testing and Education in Cancer Patients, known as ENGAGE, tests a tool developed by the team in collaboration with Optra Health, Inc., to determine if it enhances the patient experience, provides education, and helps providers. The study is supported by the Maryland Cigarette Restitution Fund Program at Johns Hopkins

Tamoxifen Resistance

Tamoxifen is a pill that is taken daily by survivors of hormone-receptor-positive breast cancer to help prevent the cancer from coming back or occurring in the other breast, and to help prevent death from breast cancer. The drug works by cutting breast cancer cells off from hormones they use to grow and spread, but it doesn't work for all patients. It has also been shown to prevent breast cancer in women at higher risk.

In collaboration with Dipali Sharma, Ph.D., M.S., Dr. Visvanathan is trying to better understand whether obesity may decrease the effectiveness of tamoxifen in some patients.

"It doesn't make sense to give it to women it won't help," says Dr. Visvanathan. "We want to understand who doesn't benefit and find other ways to help them."

New research from Dr. Sharma finds that obesity may provide an important clue to the drug's ineffectiveness. In new findings supported in part by the Avon Foundation for Women and the Breast Cancer Research Foundation, Dr. Sharma found that leptin--a molecule produced by fat cells--appears to cancel out the ef-

fects of tamoxifen. In the study, when mice were given tamoxifen, lean animals responded well and tumors regressed quickly, but when the drug was given to obese mice, tumors acted as if they had not been treated at all.

Dr. Sharma found that leptin cancels out the effectiveness of tamoxifen by turning on a cascade of cancer-promoting genes, including, in particular, Med1, which is associated with dozens of obesity-related genes. In laboratory models, when

HIGHLIGHTS

A TARGETED DRUG THERAPY, CALLED **PARP** INHIBITORS HELPS TO PREVENT DAMAGED CANCER CELLS FROM REPAIRING THEMSELVES.

TAMOXIFEN IS A PILL THAT IS TAKEN DAILY BY SURVIVORS OF HORMONE-RECEPTOR-POSITIVE BREAST CANCER TO HELP PREVENT THE CANCER FROM COMING BACK OR OCCURRING IN THE OTHER BREAST AND TO EXTEND SURVIVAL.

ADHERENCE TO SCREENING, INCLUDING MRI AND MAMMOGRAPHY, ARE HIGHLY RECOMMENDED FOR HIGH-RISK WOMEN. AN EIGHT YEAR STUDY REVEALED HOW COSTS AND ACCESS PLAYED A ROLE IN THEIR SCREENING DECISIONS.

ifen's success for obese patients with breast cancer. She and her team are studying some of these potential treatments in the laboratory as they move toward testing them in human clinical trials.

Drs. Sharma and Visvanathan are now working together to test whether obesity may reduce the effectiveness of tamoxifen through upregulation of markers such as Med1 in clinical trials of patients who were prescribed tamoxifen for prevention or treatment.

High-Risk Screening

In another prevention study, Dr. Visvanathan's team examined for the first time, adherence to screening for high risk women over an eight-year period.

Increased screening, including MRI and mammography, is recommended for these women, but Dr. Visvanathan says, "It is one thing to implement a recommendation but another to make sure it's actually happening. Guidelines are not enough."

Although mammography remained high among this patient population, the uptake of screening with MRI over the eight years was 35%, particularly in younger healthy women. More than 78% of women utilized appropriate screening for other cancers. Factors, including cost and access, may have played a role, Dr. Vis-

"It is one thing to implement a recommendation but another to make sure it's actually happening. Guidelines are not enough."

the researchers silenced the Med1 gene, tumors began responding to tamoxifen. The researchers were also able to achieve response by using the fat-secreted molecule called adiponectin or the compound called honokiol, which is derived from magnolia trees. Both agents target Med1 and were previously known to have a protective effect on cancers.

Dr. Sharma says interventions that can lower leptin, such as losing weight, or target Med1, such as the use of adiponectin or honokiol, could eventually be used to improve tamox-

vanathan says. MRI is more complicated than mammography, she adds, so the reason could also be that women don't like getting the test. The lack of adherence could delay breast cancer diagnosis and impact survival, she says.

"As we think of how we can best help people at high risk, we have to look at the obstacles to optimal care such as having regular MRI screening," says Dr. Visvanathan. "We need to be aware early so we can communicate with patients to understand the challenges and fix them."

NOTEWORTHY



In The News

Dr. Vered Stearns was recently featured in the *Jewish Times*. Read the story here: <https://bit.ly/VJSJewishTimes>

KUDOS!



John Fetting, M.D., was the inaugural recipient of the Interprofessional Practice Award by the Pharmacy Department. This award is given annually to an individual from another health profession who has worked collaboratively with Johns Hopkins Hospital pharmacists to make sustained contributions to pharmacy practice, research or education.



Researcher Combats Treatment Resistance

New faculty member **Eneda Toska, Ph.D., M.S.**, is working with the Women's Malignancies Program and Cancer Invasion and Metastasis Program to better understand how breast cancers resist endocrine (hormone directed) and other targeted therapies. Her research laboratory is focused on identifying genes that drive this resistance and the spread of cancer.

Dr. Toska came to the Kimmel Cancer Center from the Memorial Sloan Kettering Cancer Institute, where she trained in the world-renowned laboratory of Jose Baselga, M.D., Ph.D., who passed away in 2021. Dr. Baselga, who was considered a leader in the development of precision (individualized) medicine using targeted therapies, played a key role in the development of the breast cancer drugs trastuzumab (Herceptin) and pertuzumab (Perjeta).

Working in Dr. Baselga's laboratory, they sequenced thousands of tumors, revealing genetic drivers involved in turning genes on and off, and she characterized them in breast cancer models to understand how they contribute to treatment resistance.

Her Kimmel Cancer Center lab continues to characterize mechanistically the genetic drivers of resistance, focusing on epigenetic (chemical alterations to genes) regulators and the spread of breast cancer.

Apart from her efforts in the lab, one of Dr. Toska's goals is to build a repository of breast cancer samples obtained during biopsy. Dr. Toska will use the samples to build organoids--tiny, natural replicas of human or mouse breast cancers--to better understand the mechanisms of how a specific cancer originates and grows and as a unique way to test responses to treatments, including combinations of drugs. The repository will also use tissue samples to search for new drivers of therapy resistance by performing genetic sequencing and transcriptomic sequencing, which identifies which genes and gene signatures are activated. Research done in her lab will validate these findings in breast cancer cellular models and identify the mechanism of by which these drivers mediate therapy resistance. Her ultimate goal is to find ways to target these drivers with treatment to benefit patients.

"This will help us link genomics with clinical outcomes and identify new treatment approaches," says Dr. Toska. She hopes her work will reveal ways they can help patients revert resistance, returning the tumor to a treatment responsive state.

HOPE AT HOPKINS

A Multidisciplinary Clinic for Those Living with Metastatic Breast Cancer

The Kimmel Cancer Center announces a new specialized clinic for patients with metastatic breast cancer. The clinic offers a half-day visit with experts in wellness, symptom management and the latest advances in the management of the disease. Patients receive a comprehensive care plan that combines recommendations for well-being, future treatment options, and education. To learn more email: BreastCancerHope@jhmi.edu



Christine Hodgdon was diagnosed with stage 4 metastatic breast cancer in 2015, at the age of 34.

PATIENTS WHO INSPIRE RESEARCH

The Johns Hopkins INSPIRE Breast Cancer Research Advocacy Program is a collaboration among breast cancer survivors, researchers and physicians in the Kimmel Cancer Center's Women's Malignancies Program. Its aim is to inform bench-to-beside research.

INSPIRE stands for "influencing science through patient-informed research and education." The goal, says Co-Scientific Director **Vered Stearns, M.D.**, is a leading research advocacy training program that promotes innovative and patient-informed research to improve treatment and well-being for those with breast cancer of all stages and for those at risk of breast cancer development or recurrence.

They are seeking broad membership, including representatives from minority and other underserved populations. Patients who are stable or at least six months from diagnosis, caregivers, or others who live in the mid-Atlantic region and are interested in advocacy, are invited to join. Members will be asked to attend videoconference meetings to learn about breast cancer science, and to have a voice in driving research aimed at improving therapies and survival.

INSPIRE is led by Dr. Stearns; **Daniele Gilkes, Ph.D.**, co-scientific director; **Jennifer Sheng, M.D.**, medical oncologist; and patient advocates **Christine Hodgdon, M.S.**, and **Samantha Horn**.

Those Who INSPIRE Us

Christine was diagnosed with stage 4 metastatic breast cancer in 2015 at age 34. She had a complete response to her treatments and decided to leave her professional career as a conservation biologist to become a full-time patient advocate.

"I endured all of my treatments, which resulted in a complete response, and I currently have no evidence of disease in my body," she says. "I am still a stage IV patient and always will be. I can never be "upgraded" to stage 1, 2 or 3, or even say that I'm in remission. I am merely stable for now. Every six months, I am scanned to monitor any progression of my disease. I will be on treatment for life, with monthly targeted therapy infusions every three weeks, as well as hormone therapy, to manage my metastatic breast cancer."

Christine created her own search algorithm to capture all possible clinical trials for metastatic breast cancer patients and launched TheStormRiders.org, a website that includes a searchable trial and drug database, a calendar of events, and research articles specific to metastatic breast cancer. She also co-founded GRASP, or Guiding Researchers & Advocates to Scientific Partnerships, a program aimed at bridging the gap that often exists between scientists and patient advocates.

Samantha was diagnosed with stage 2 estrogen receptor-positive breast cancer in 2014 when she was

26 years old. She learned she had a BRCA1 mutation — a gene mutation that increases the risk of developing breast and other cancers — after her diagnosis. After completing surgery and chemotherapy, she wanted to give back to the cancer community. She became a Young Advocate with Living Beyond Breast Cancer in 2016. Since training with Living Beyond Breast Cancer, she reviewed grants for the Department of Defense Breast Cancer Research Program and joined the Johns Hopkins Medicine Young Women's Advisory Committee for their Breast Cancer Program. Currently, Sam is a member of Young Survival Coalition's Respected Influencers through Science and Education class of 2020 and continues advocacy efforts at Johns Hopkins.

Other advocacy includes giving testimony to the Maryland State Senate Finance Committee to lobby for Maryland insurers to cover the cost of fertility preservation and media coverage for the same bill. Her personal and professional interests came together when she accepted a position as an adolescent and young adult patient navigator with the Ulman Foundation, where she fostered a community of support for young adults ages 15–39 impacted by cancer. She is currently the outreach coordinator for the Lapidus Cancer Institute at LifeBridge Health in Baltimore, Maryland.

Join them or learn more by emailing Chodgdon513@gmail.com

SAGE STRONG

The Johns Hopkins Women's Wellness and Healthy Aging Program offers a holistic and individualized approach for women living with breast cancer.

A multidisciplinary team of specialists in women's cardiology, bone health, sexual health, gastroenterology, psychiatry and more provide information and guidance on health, wellness and quality of life. Our patient navigator works with patients and doctors to coordinate consultations with the specialists.

To learn more about the Women's Wellness and Healthy Aging Program please visit our website <https://bit.ly/31WomensWellness> or email our patient navigator at womenswellness@jhmi.edu.

Women's Wellness and Healthy Aging Program



From your initial consult through continued monitoring, your health is our top priority

We are **SAGE** - Strong in **AGE**ing

Women's Wellness and Healthy Aging Program



Our patient navigator facilitates consultations and helps you establish a relationship with providers

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Women's Wellness and Healthy Aging Program

You want to feel your best, but you don't know where to start. We can help.



We are **SAGE** - Strong in **AGE**ing

Women's Wellness and Healthy Aging Program



Streamlined scheduling, preconsultation testing, and a patient navigator mean I can spend less time managing my healthcare

We are **SAGE** - Strong in **AGE**ing

Help Us Make a Difference

Each contribution to 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 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 cancer and support survivors.

You may designate a gift to a specific faculty member.

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