

Prevention Matters

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CHANGE IN STATUS FOR THE NBN GENE. IT IS NO LONGER CONSIDERED TO HAVE A BREAST CANCER RISK. *by Kim Rainey, MS, MEd, LCGC, Genetic Counselor*



Genetics is a dynamic field and as more people pursue genetic testing, our understanding of the cancer risks linked to various gene mutations is evolving. One of the genes we used to think had an increased risk for breast cancer, the NBN gene, has now been "downgraded" with no statistically significant link to breast cancer. In the past, a woman with an NBN mutation was considered to have

New England Journal of Medicine (N Engl J Med 2021; 384:440-51). It confirmed the increased risk in most of the well-known breast cancer genes, however the NBN gene didn't make the grade.

Although the NBN gene is no longer a factor in cancer risks, it is still important for family planning since two individuals who both carry an NBN gene mutation have a 1 in 4 chance of having a child with Nijmegen breakage syndrome (NBS). This is a rare recessive condition that can present with sensitivity to radiation, a small head, delayed growth, immunodeficiency and cancer risks.

In the coming years, we will continue to refine our knowledge of cancer susceptibility genes and the screening guidelines may change. If you carry a cancer gene mutation, you may want to check with your genetic counselor from time to time to see if there are any changes that apply to you. If you are currently being seen in the high risk clinics, your clinician will inform you of any updates. The Risk Assessment team at Fox Chase is a valuable resource for you and your family, so don't be shy about reaching out to us.

enough of a risk to warrant the option of adding breast MRI to her annual screening. Based on the newest NCCN guidelines, there is no longer a recommendation for increased breast cancer screening for NBN mutation carriers. It may be that the family history is still strong enough to warrant the addition of a breast MRI, however an NBN pathogenic mutation alone is no longer in the "high risk" category. This news can be unsettling to women who carry an NBN mutation so let's look at how we got to this point.

As we look back at the history of genetic testing, the BRCA genes were discovered with the help of families with strong histories of breast and ovarian cancer. In the early days, only individuals with cancer or from families with a strong history of cancer were referred by their doctors for genetic testing. Gene mutations were identified in these families and it was assumed that the mutations explained the cancers. With the availability of affordable expanded gene panel testing, genetic testing has become more widespread and we are learning that some of these gene mutations are more common in the population than we thought and not necessarily the explanation for the cancers in families.

A large population-based case-control study with 30,000+ women with breast cancer (cases) and 30,000+ women without breast cancer (controls) was performed through the CARRIERS consortium to revisit the risk for breast cancer in 28 cancer-predisposition genes. That study can be found in the



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Mary Daly Receives National Comprehensive Cancer Network's 2021 Rodger Winn Award



Mary B. Daly, MD, PhD, FACP, professor in the Department of Clinical Genetics and director of the Risk Assessment Program at Fox Chase Cancer Center, recently received the National Comprehensive Cancer Network's (NCCN) Rodger Winn Award.

The Rodger Winn Award is given annually to one NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) panel member who exemplifies commitment, drive, and leadership in developing evidence-based guidelines, according to the NCCN.

The award is named in honor of Rodger Winn, MD, who in addition to being the founding editor-in-chief of JNCCN—Journal of the National Comprehensive Cancer Network, was a dedicated advocate for patients and healthcare providers. Winn continued to help patients

through their cancer journeys, even during his own cancer diagnosis and treatment, until his death in 2007.

"I had the opportunity to know Rodger early in my career, and his example has always been a guiding force for me. He was a kind, generous, and humble man who at the same time had a passion for elevating cancer prevention research to new heights. Nothing would mean more to me than to be able to be a role model to others in the field of cancer prevention as Rodger was to me," said Daly.

Dr. Daly was recognized with the award for her leadership in developing the Genetic and Familial High-Risk Guidelines for hereditary cancers, a resource that is widely used by the genetics and oncology community. She is also the founding chair of the NCCN Guidelines Panel for Genetics and Familial High Risk Assessment: Breast, Ovarian, and Pancreatic, as well as a former member of the Breast Cancer Risk Reduction Panel and the Breast Cancer Screening and Diagnosis Panel.

WELCOME ABOARD

Alison McManus, Clinical Genetics Intake Coordinator

I moved to the United States from Ireland in 2013. I previously worked as a nurses' aid on the 4th floor at Jeanes Hospital before joining the Fox Chase Cancer Center outpatient ambulatory team in 2016. During that time, I supported the various outpatient clinics in assisting with patient care needs as well as recent COVID testing operations. I am very excited for this new opportunity to learn a new role as a clinical genetics intake specialist within the Department of Clinical Genetics at Fox Chase/Temple Health.



Chau Nguyen, MS, CGC, Genetic Counselor

I am very excited to join the Risk Assessment Program at Fox Chase and return to the place that helped cultivate my passion for cancer genetic counseling.

I was born and raised in Newark, Delaware and earned my Bachelor of Arts in Psychology from the University of Delaware. After studying at UD, I relocated to Glenside, Pennsylvania where I went on to earn my Masters of Science in Genetic Counseling from Arcadia University. It was through my studies at Arcadia that I had my first encounter with the Fox Chase Cancer Center as a graduate student learning about cancer genetics.

Since earning my Master's degree and becoming a licensed certified genetic counselor I have been a clinical cancer genetic counselor for the past three years at Christiana Care in Delaware. Now, as I join Fox Chase's Risk Assessment Program, I am honored to be working with the team who once taught me the tremendous impact genetics can have on cancer risk assessment.





Adjuvant Olaparib for Patients with BRCA1 or BRCA 2-Mutated Breast Cancer

Mary Daly, MD, PhD, FACP

Polymerase inhibitors (PARP) are drugs used to target certain cancers, particularly in patients with mutations in BRCA1 or BRCA2. They have been shown to prolong survival in BRCA-related ovarian cancer. A new study looked to see if these drugs could be used to reduce recurrence in patients with BRCA1 or BRCA2 germline mutation associated early breast cancer.

This randomized trial involved patients with a BRCA1 or BRCA2 germline pathogenic or likely pathogenic mutation that had human epidermal growth factor receptor 2 (HER2) negative early breast cancer. These patients had received local treatment and neoadjuvant (therapy given before the main treatment) or adjuvant (therapy given after primary treatment) chemotherapy. All patients had to have "high-risk" disease, such as large tumor size, positive lymph nodes, or poor response to initial chemotherapy. Patients were randomly assigned to one year of the drug, olaparib, or a placebo.

A total of 1836 patients were randomized. Researchers found that the 3-year invasive disease free survival was 85.9% in the olaparib group and 77.1% in the placebo group. The 3-year distant disease free survival was 87.5% in the olaparib group and 80.4% in the placebo group. Olaparib was associated with fewer deaths than placebo.

Among this patient population, adjuvant olaparib after completion of local treatment and chemotherapy was associated with longer survival free of invasive or distant cancer than placebo. This is the first trial to show an advantage to using olaparib in breast cancer in the adjuvant setting.

Read the article:

www.nejm.org/doi/full/10.1056/NEJMoa2105215

SUMMER STUDENT'S PROJECT: Emma Riggs Preventive Behaviors and Attitude toward Current and Emerging Prevention Options among Patients with Lynch Syndrome

Fox Chase Cancer Center continues to mentor undergraduates from diverse colleges and universities by engaging them in summer research projects.

This past summer, Emma Riggs was given the opportunity to work with Dr. Michael Hall in the Department of Clinical Genetics. Emma is currently a sophomore at Franklin & Marshall College. She plans to major in Neuroscience on the pre-med track with a minor in Spanish. She worked on a project looking at screening behaviors in patients with Lynch Syndrome (LS) and their perceptions of risk and disease.

LS is one of the most common hereditary cancer syndromes affecting approximately 1/300 in the general population. LS results from a germline mutation in one of the five mismatch repair genes: MLH1, MSH2, MSH6, PMS2, or EPCAM. Patients with LS are more likely to develop multiple types of cancer over their lifetime including colorectal, endometrial, ovarian, stomach, urinary tract, and others. However, the highest risk is associated with colorectal and endometrial cancer (for women).

While LS is fairly common, treatment and prevention options are limited and ever-changing. The PreventLynch survey was used to collect data regarding patient perceptions of risk and disease severity, current screening behaviors, and attitudes toward current and emerging prevention options. The sample included 116 individuals with LS, of which 76% were female and 96% self-identified as white. The mean age was 52.7 years.

After analyzing survey results, the data suggested that patients with a personal cancer history versus those with a familial cancer history have strong, but different perceptions of risk and disease. Those with a personal cancer history felt

they were at higher risk to developing a new cancer or pre-cancer related to LS in the next 5 years, while patients with a familial cancer history had stronger perceptions of LS disease severity. Additionally, patients with a personal cancer history were more likely to pursue cancer screening options and maintain stricter screening intervals of cancer.

The survey results found that high prevention reassurance of colonoscopy outweighed side effects and inconvenience (uptake for colonoscopy screening was >96%). On the other hand, daily aspirin, a proven prevention method for LS, was shown to provide low prevention reassurance which ultimately hinders uptake of this prevention method (only 35% of patients took daily aspirin and only 76% of those taking aspirin did so specifically for LS prevention). Results also suggest that up and coming vaccine and immunotherapy trials may be less attractive to patients than exercise or diet-focused trials. The vaccine and immunotherapy trials had higher perceived side effects and inconveniences compared to perceived prevention benefits. The exercise and diet-focused trials had a higher acceptability of side effects and lower perceived inconveniences.

These data will be presented at The Collaborative Group of the Americas on Inherited Gastrointestinal Cancer (CGA-IGC) conference in November 2021.



Importance of Diversity in Clinical Research

Interview with Michael Hall, MD, MS, a professor in the Department of Clinical Genetics and Evelyn González, MA, Sr. director of the Office of Community Outreach at Fox Chase. [Interview is modified for brevity and clarity]

Underrepresentation of racial and ethnic minority populations in clinical/medical research continues to be an issue in the United States. A person's race, ethnicity, sex, and health factors play critical roles in developing safe and effective treatment options for people of diverse backgrounds.

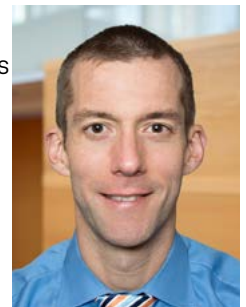
Members of many minority groups are still hesitant to be a part of research, even though they face an unequal burden of cancer with poorer outcomes. There are many barriers to participation in research, such as the lack of awareness/understanding, mistrust in the healthcare system, poor communication from healthcare providers, and more.

Researchers can work to improve diversity in clinical research by providing education, building trust with patients, and creating partnerships and collaboration with the community.



Why is diversity in clinical/medical research so important?

Dr. Hall: Sometimes members of the public underappreciate that most of the advances we have in medicine today were made because we carefully studied a particular problem, such as a new drug or a surgical technique, in our patients. We learned the answers to those questions and developed our best clinical pathways by engaging our patients in research, and working together to improve care. But one thing that has been a challenge is that most medical research has generally been conducted in patients who are much younger than average, and in mostly Caucasian patients. This is partially due to a greater willingness of younger and Caucasian patients to participate in research, but the outcome of this gives us an incomplete picture of how a particular therapy or procedure might work in all our patients. In the coming years, the scientific community would like to improve participation of more diverse patients in research so that the findings and benefits of research are relevant to everyone.



Would you please give an example from the cancer world?

Dr. Hall: Triple negative breast cancer (TNBC) is a very aggressive form of breast cancer, but one that notably affects young Black women. To study this disease in non-Black women is still valuable, but we have to understand that there is something about the causes or risks of TNBC that appears to be specific to young Black women that may benefit our understanding of the disease in all women. To understand this disease, we need to understand this connection. We need to study whether there are currently unknown but modifiable environmental risk factors or biological factors that may be specific to young Black women. If we really want to help the population who is getting hurt the most by this disease, we need to enroll those individuals in the research of this disease.

Why are racial/ethnic minorities reluctant to participate in clinical research?

Evelyn González: There are several factors that impede the process of people joining clinical research:

- A lack of awareness about research and the research process. If we help the community understand that today's treatments are a result of yesterday's clinical trials, we have more receptivity where people are willing to listen.
- Cultural perspective and mistrust. The history of clinical trial abuses can still negatively impact our ability to recruit. When people go home and they are with older family members who have this historical perspective and they say, "Oh, honey, you don't want to do that." Who are they going to listen to? Will they trust a person whom they know and love, or person who they just met two hours ago? This why sharing information about their rights as participants and patient protection measures is critical. When possible, include family members in the discussion. Over the years we have found that when we educate participants and allow for active discussion, their intent to participate increases.
- Health literacy. Explaining research using a lot of medical jargon intimidates patients. Also, the informed consent forms are often written at higher educational levels that include medical and legal terms that often scare people.
- Language. If a person is limited English proficient and there is no bilingual staff to engage the patient and explain in their primary language, that is a major barrier. Having onsite certified medical interpreters is key.



Importance of Diversity in Clinical Research *(Continued)*

Dr. Hall: I would like to add a couple of other factors that are obstacles for participation:

- People do not always have access to the medical facilities where clinical trials are conducted, and the lack of insurance can be a huge barrier.
- Often patients need more support in order to participate in research that does not always exist in the immediate situation such as child care, reliable transportation or time off from work.

In addition, when you consider patient, family and community views about whether clinical research participation has value, the patient might decide that the barriers outweigh the benefits of participation.

How do we engage the racial and ethnic minority population in clinical research?

Evelyn González: It is complex, it is time consuming, but it is also very rewarding. For years, the Office of Community Outreach (OCO) at Fox Chase has worked with diverse organizations, faith-based institutions, businesses and health care providers to let people know about cancer, health issues and research opportunities and to share our goal of reducing cancer health disparities. OCO provides cancer education, weaving in messages about research. Recently, we trained a group of African-American community ambassadors on cancer research. The goal is to have the ambassadors educate their community networks about the importance of considering research participation. We went through a 7- week training where we brought in our faculty to talk about research and clinical trials, and not only presented data but we address the issue of past abuses using *The Immoral Life of Henrietta Lacks*. We followed-up by bringing the group to the laboratory to see the cells, how we consent to obtain the samples, collect and store our samples. It gave them a better appreciation for the process and the respect we have for these samples. Some of the conversations were difficult, however, it also provided the opportunity to discuss the scientific advances these cells have contributed to. For example, Dr. Baruch S. Blumberg won the Nobel Prize in Medicine for his discovery of the hepatitis B virus in 1967. He and his colleagues developed the blood test that is used to detect the virus, and invented the first hepatitis B vaccine in 1969 here at Fox Chase Cancer Center.

To participate in a clinical research, talk to your healthcare provider and let them know that you're interested in learning more about research opportunities. You can visit: [ClinicalTrials.gov](https://www.clinicaltrials.gov). This website is maintained by the government and lists active trials for many different diseases and illnesses.

Fox Chase Receives a Grant from The MANNA Institute to Investigate Intersection of Nutrition and Cancer Care



Researchers at Fox Chase Cancer Center have been awarded a \$50,000 research grant from the MANNA Institute to measure the impact of a medically tailored meal program in patients with a colorectal cancer diagnosis.

The grant is one of the first grants in the history of the MANNA Institute and are funded by the institute's founding donors. The MANNA Institute studies the impact of nutrition on the health of people with serious illnesses. It leads research, educates healthcare providers and patients, and shares findings and best practices for improved service delivery and healthcare transformation.

Drs. Rishi Jain and Michael Hall, GI oncologists and Kara Stromberg, a clinical manager of nutrition and food services at Fox Chase Cancer Center, are the principal investigators for the research study, "**A Medically Tailored Meal Program to Improve Chemotherapy Tolerance in Patients with Colorectal Cancer: A Pilot Study.**"

The study's goal is to evaluate whether receiving MANNA's medically tailored home-delivered meals and nutrition counseling can help improve the outcomes of patients with colorectal cancer undergoing chemotherapy. The study will measure unique health outcomes, such as malnutrition, sarcopenia (loss of skeletal muscle mass), chemotherapy tolerance, and quality of life.

The research project is expected to start patient enrollment in early December, 2021.





VIRTUAL PATIENT EDUCATION EVENT

A virtual patient education event, **“Understanding Hereditary Risk: A Virtual Event for Patients, Families and Friends of Fox Chase Cancer Center”** was hosted by the Department of Clinical Genetics on June 22, 2021 through the Fox Chase Cancer Center Facebook page. This upbeat presentation provided up to date information about hereditary risk for breast, prostate, gastrointestinal and other cancers, as well as information on lifestyle factors for cancer prevention, and some insight into the future of genetics and research.



Our speakers included: Kristen Whitaker, MD, MS; Elias, Obeid, MD, MPH; Michael J. Hall, MD, MS; Hannah Campbell, ScM, LCGC; Rishi Jain, MD, MS, DABOM; and Mary B. Daly, MD PhD.

A special thank you to our exhibitors: AbbVie, Caris, Foundation Medicine, Invitae, Myriad Oncology, Novartis, Pfizer Oncology, Promega, Puma Biotechnology and Tempus.

The following advocacy groups were part of this event and offer education and support for those with hereditary cancer syndromes such as Hereditary Breast and Ovarian syndrome, Lynch syndrome, and others: AliveAndKickn, Bright Pink, FORCE and Lynch Syndrome International (LSI).

In case you missed this informative event, please visit: [facebook.com/foxchasecancercenter/videos/971663073398444/?_rd=1](https://www.facebook.com/foxchasecancercenter/videos/971663073398444/?_rd=1)

Dr. Obeid, Director of Breast, Ovarian, and Prostate Cancer Risk Assessment answered the following questions asked by patients during the event.

Can female children of men with prostate cancer risk have higher risks of other cancers?

It is estimated that between 5 and 10 percent of cancers diagnosed are related to a genetic predisposition, which is from inherited genetic mutations from one or both parents. Men who have a genetic mutation can pass that mutation to both their male and female children.

There is a 50 percent chance that a child will inherit the mutation that their father carries. Different genetic mutations linked to cancer predisposition increase cancer risk to certain cancers. Our knowledge of different cancer risks continues to evolve. For example, a man with a BRCA mutation is at higher risk for prostate cancer, pancreatic cancer, melanoma and breast cancer. A female with a BRCA mutation would be at higher risk for breast, ovarian, endometrial, melanoma and pancreatic cancers.

Family history is important to determine if you have a higher risk for cancer. Talk with your doctor if:

- Two or more relatives on either your mother's or father's side of the family have cancer
- First degree relative (parent, sibling, child) diagnosed before age 50 with ovarian, uterine, breast or colon cancer
- A male relative had breast cancer
- Eastern European or Ashkenazi Jewish ancestry

<https://www.cdc.gov/cancer/family-health-history/index.htm>

What is the recommended screening for breast cancer for men that are BRCA gene positive?



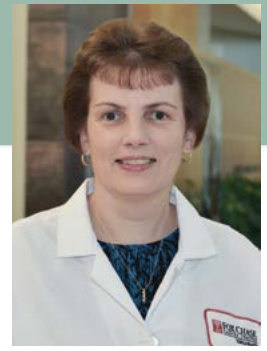
Since less men get diagnosed with breast cancer, compared to women, research related to screening for breast cancer in men is limited. It is well known that male carriers of BRCA gene mutations are at a higher risk for breast cancer compared to men without a BRCA mutation. Male BRCA 1 gene carriers are at a 2% lifetime risk for breast cancer and men who are BRCA 2 gene carriers are at an 8% lifetime risk. The average man without a gene mutation is only at a 0.1% risk for breast cancer. Men with a BRCA mutation are also at increased risk for prostate cancer, pancreatic cancer, and melanoma.

The National Comprehensive Cancer Network (NCCN) guidelines (v 1. 2022) currently recommend the following for male BRCA carriers:

- Breast self-exam training and education starting at age 35 years.
- Clinical breast exam, every 12 months, starting at age 35 years.
- Consider annual mammogram screening in men with gynecomastia (overdevelopment or enlargement of the breast tissue in men) starting at age 50 or 10 years before the earliest known male breast cancer in the family (whichever comes first).

Having Healthy Gut Bacteria Is Important for Overall Health and Cancer Prevention

Margie Clapper, PhD, Professor and Co-Leader, Cancer Prevention and Control Program



One of the trendy health topics right now is gut health. Fashionable or not, it's an exciting area of research. Scientists are making new discoveries about the role of the gut microbiome and how it's related to disease—including cancer.

What is a microbiome?

A microbiome is a diverse community of organisms. This population includes trillions of bacteria, fungi, and other organisms. And like any neighborhood, each inhabitant plays an important role within the community.

"These are microorganisms that we live with every day," explained Margie L. Clapper, PhD, deputy scientific director and a leader in cancer prevention and control at Fox Chase Cancer Center. "They inhabit our bodies, and we maintain partnerships with them. They're needed for a healthy balance."

Several areas of the body have unique microbiomes. You'll find these communities on the skin, in the vagina, in the mouth, and in the gut. Most microbes, however, are found in the gut.

How can a gut microbiome contribute to disease?

We need a healthy balance of good and bad bacteria to maintain our immune system. If that balance is disrupted in the gut, if there are too many bad bacteria, it may cause an immune reaction that triggers inflammation, which may lead to diseases, such as colorectal cancer.

"The inner surface of the colon is covered in a mucus layer," Clapper explained. "If bacteria have an opportunity to invade that and get close to tissue, if that defense is missing, it can start an inflammatory reaction, which has the potential to encourage tumor growth."

Although the gut microbiome may be linked to diseases like colorectal cancer, gut health impacts more than just the gastrointestinal system.

"With gut microbiomes, we know that there are effects that go far beyond the gut," Clapper said. "There's data to suggest that when cancer metastasizes, the tumor cells take the local microbiota with them—it's a passenger that most likely helps establish tumor growth at the distant site. In general, the gut microbiome can impact many other parts of the body."

What's happening with research into the gut microbiome and cancer?

Leading-edge studies are exploring how gut bacteria operate. Research topics include:

- What specific bacteria may help colorectal cancer grow and spread
- How gut bacteria may impact other cancers, like liver and skin cancer
- How to offset the disruption that some cancer treatments, such as chemotherapy and radiation therapy, can have on the healthy gut microbiome

How can I take care of my gut microbiome?

Every person's microbiome is different. But eating fruits, vegetables, and other foods high in fiber can help support the good bacteria in your gut. So can eating foods like yogurt and sauerkraut, which contain beneficial bacteria. Probiotic supplements can also help support a healthy balance in the gut microbiome. But since there are many different types of probiotics available, it is best to talk to your doctor before taking one.

Stress can also have a negative impact on the gut microbiome, Clapper said. So reducing stress may make for a better gut environment too.

A healthy lifestyle can help make your gut happy and have a positive impact on your overall wellness.

Creamy Broccoli Apple Salad

This recipe is a delicious blend of fruits, veggies and protein meant to help someone living with cancer meet their basic nutritional needs. Greek yogurt is also high in probiotics and whey protein, which may play a role in immune system support. Due to the nutrient density of this snack, it is perfect for those with reduced appetite.

- 4 cups broccoli florets
- 1/2 cup carrots, shredded
- 1/2 red onion, sliced thin
- 2 apples, diced
- 1/2 cup pecans, chopped
- 1/2 cup dried cranberries
- 1 cup plain Greek yogurt
- 2 Tbsp. lemon juice
- 1 Tbsp. honey
- Salt and pepper, to taste



Directions:

1. In large bowl, combine broccoli, carrots, onion, apples, pecans and cranberries.
2. In separate bowl, whisk together yogurt, lemon juice and honey.
3. Combine yogurt mixture with vegetable mixture and toss well. Season to taste with salt and pepper.
4. Chill until ready to serve.

Makes 8 Servings (1 cup). Per serving: 140 calories, 6 g total fat (1 g saturated fat, 0 g trans fat), 5 mg cholesterol, 20 g carbohydrates, 5 g protein, 3 g dietary fiber, 25 mg sodium, 15 g sugar, 2 g added sugar.

Notes: Full fat Greek yogurt can be used to promote additional caloric intake for weight gain. Adding more lemon juice may also improve the taste profile for someone with mild dysgeusia [altered sense of taste].

Prevention *matters*

The Department of Clinical Genetics offers one of the most comprehensive risk assessment programs in the Philadelphia region. It encompasses all of Fox Chase Cancer Center's clinical services for people at risk for cancer, as well as innovative research in the areas of cancer prevention and genetics.

CONTACT THE RISK ASSESSMENT PROGRAM:

1-877-627-9684 | foxchase.org/rap | rapinfo@fcc.edu

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CALENDAR OF EVENTS:



3rd Annual Metastatic Breast Cancer Conference
Sunday, November 14 – Virtual Event
<https://www.komen.org/>

Fox Chase Cancer Center's Lippincott Resource & Education Center (REC) invites you to attend upcoming virtual free education sessions:

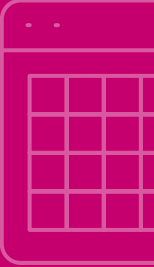
THE HEART OF THE SPIRIT

Wednesday, November 10, 2021 | 1:00 pm – 2:00 pm |

NUTRITION: MYTHS VS. TRUTHS

Wednesday, December 1, 2021 | 12:00 pm – 1:00 pm |

To register, or more information,
please call **215-214-1618**
or email: **RECstaff@fcc.edu**.



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