Prevention Matters

| FOX CHASE CANCER CENTER RISK ASSESSMENT PROGRAM PUBLICATION | FALL/WINTER 2023

Fox Chase Cancer Center's Dr. Mary Daly Receives Inaugural Impact Award from Basser Center for BRCA

Mary Daly, MD, PhD, FACP, a professor in the Department of Clinical Genetics and the Timothy R. Talbot Jr. Chair in Cancer Research, has been recognized as the first recipient of the Basser Impact Award from Penn Medicine's Basser Center for BRCA. From the start Daly knew her career would lead to science. Raised in Bridgeport, Connecticut she fell in love with Biology while in high school. She continued to pursue her love for science in college, obtaining a bachelor's degree in biology from an all-women's college in New Rochelle, New York. Shortly after finishing school, she decided to put her career in science on pause; she and her husband accepted an opportunity to teach high school students in Kenya as a way to use their education to help a country that did not have the same educational resources.

After working in Kenya for 3 years, where she had her first two children, her family moved back to the United States. With a greater appreciation of the importance of public health afforded by living in a country dealing with widespread infectious diseases, she went back to school receiving her masters and doctorate degrees in epidemiology at the School of Public Health, University of North Carolina at Chapel Hill.

After completing her doctorate in epidemiology, she was offered a position to work in Geneva, Switzerland, with the World Health Organization as an epidemiologist. At the same time, she applied and was accepted into medical school at the University of North Carolina, Chapel Hill. She stated, "I realized that epidemiology teaches you a lot about study design and statistics, but it doesn't teach you about the diseases that you're studying. I realized that medical school would give me a deeper understanding of health and disease so that I would be able to ask the right questions in my research. So, after much heart wrenching and hand wringing, I went and sent a telegram to World Health Organization and said I couldn't accept the position and the rest is history."

After finishing medical school, internal medicine training and her medical oncology fellowship, she started work as an oncologist at the Air Force hospital in San Antonio, Texas. In her time there, Dr Daly notes one of the proudest accomplishments of her career was being one of the eight medical oncology physicians who worked to establish the bone marrow transplant unit at the Air

Mary Daly and Susan Domchek, a director of the Basser Center for BRCA.

Force hospital, something that was nonexistent before the team's efforts. "Nowhere in the Department of Defense, was there a hospital that offered bone marrow transplantation. They would have to go out into the community, which costs a lot of money. We each spent two months at the Fred Hutchinson Center in Seattle, which is the premier bone marrow transplant program in the world learning how to do bone marrow transplants. We came back to the Air Force Hospital and established a bone marrow transplant unit and started doing approximately one hundred transplants a year, which is pretty good volume. That was a tremendous learning experience, not just the clinical care of transplant patients, but how to set up such a complicated program. I think it helped me when I was ready to set up a program at Fox Chase in genetics."

At the start of Daly's career at Fox Chase in 1989, genetics had not been incorporated into the care of cancer patients. "I had been studying the work of Henry Lynch." Henry Lynch was an American physician who is known for his description of the clustering of certain cancers in families. "At first his work

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FOX CHASE CANCER CENTER
TEMPLE HEALTH

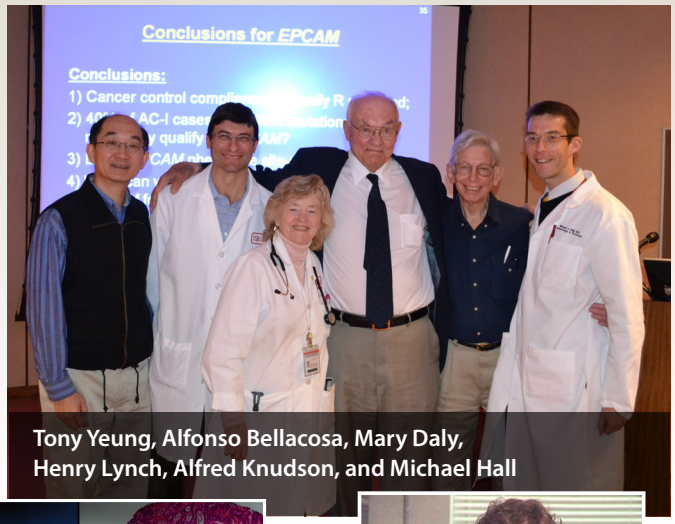
IN THIS ISSUE

went unnoticed, but it caught my attention, and I said 'somehow, I want to be able to weave genetics into my research program'. It was difficult because no one was doing cancer genetics in the clinical setting." Everything changed, by October 1990 when the Human Genome Project launched, and by 1994 the BRCA1 mutation was identified.

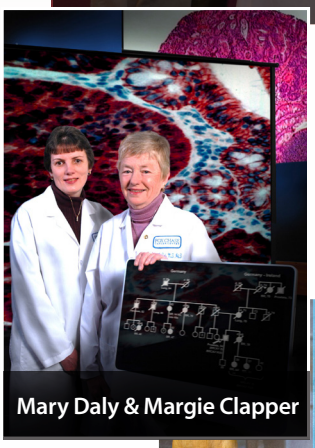
It was 1991 when Dr Daly started collecting her own family registry. The program, which initially focused on assessing ovarian and breast cancer risk, now also includes risk assessment for several types of cancer, including prostate, gastrointestinal, lung, melanoma, endocrine and kidney. The program provides education, individualized counseling, genetic testing, and screening to high-risk patients." In 1995 the National Cancer Institute was looking for researchers who had a cohort of families and thus the Breast Cancer Family Registry (BCFR) cohort started. It's an international cohort of breast cancer families which to this day continues to make important contributions to breast cancer prevention, early detection, and treatment.

The Basser Center for BRCA at Penn Medicine's Abramson Cancer Center was established in 2012 by University of Pennsylvania alumni, Mindy and Jon Gray. It was named in honor of Faith Basser, Mindy's sister who died of BRCA-related ovarian cancer at the age of 44. The center was created with the goal of advancing genetic research and improving the lives of those who are carriers of the BRCA mutations. The Basser Center was able to aid in accelerating BRCA-related cancer research and the development of targeted therapies.

"Receiving this award helps me realize the impact that setting up one of the first risk-assessment programs for cancer prevention even before we knew about the cancer genes can have on families and their health care providers."



Tony Yeung, Alfonso Bellacosa, Mary Daly, Henry Lynch, Alfred Knudson, and Michael Hall


Mary Daly & Margie Clapper

Meet Our New Team Members

Sonya Nosikovskaya, Clinical Genetics Intake Coordinator

I was first introduced to cancer genetics a little over 6 years ago. I immediately became fascinated. I worked closely with the genetic counselor at Holy Redeemer and my fascination grew more and more. I did a little research and found that Johns Hopkins offered a genetic assistant training program and I immediately signed up. The more I learned, the more I fell in love and have continued on this path since. My love for this field grew more as I worked closely with the genetic counselor at Doylestown as well and have now made my way to Fox Chase Clinical Genetics program. I hope to grow even further in the field of cancer genetics. Some of my hobbies include reading fantasy, drawing, and writing. I love anime and comic books. I also attend at least 2 comic conventions per year and have a tradition of buying 1 plushie at each one.

Deb Grace, Research Assistant

I am very excited to join the Clinical Genetics department here at Fox Chase. I will be working as the project coordinator for the Breast Cancer Family Registry (BCFR) and the Prostate Risk Assessment Program (PRAP). Prior to coming to Fox Chase, I completed a Bachelor of Science from Penn State University. During my time at Penn State, I worked as a research assistant in a mathematical modeling lab researching malaria, a research assistant in developmental psychology, and a pharmacy technician. I am excited to learn and grow with the RAP team and provide research support to the department.

RESEARCH UPDATE IN RENAL CELL CARCINOMA (RCC)

By Elena Demidova, MS and Sanjeevani Arora, PhD

Renal cell carcinoma (RCC) is a type of kidney cancer that affects numerous people worldwide each year. However, there is a rising incidence of early-onset RCC in younger individuals, particularly in the United States, before the age of 50 years, and the reasons for its younger onset are still largely unknown.

To investigate the genetic causes of early-onset RCC, Fox Chase researchers conducted a study in collaboration with the Fox Chase Cancer Center Risk Assessment Program, focusing on early-onset RCC patients who did not have known inherited genetic mutations. The study revealed that a significant number of these patients had variations in genes that repair damage to DNA and aid in dividing DNA (i.e. DNA replication), particularly DNA polymerase genes. By functional evaluation of the DNA polymerase variants, researchers showed that these variant polymerase(s) have differences in their biochemical activity, increased tendency for replication errors, and thereby increased mutational burden in renal tumors.

Furthermore, the study discovered that peripheral blood lymphocytes (a type of white blood cell that circulates the blood) carrying such variants were sensitive to mutagens (agents that can cause mutations or make changes in the DNA). This suggests that screening patient lymphocytes could provide insight into the mechanisms of early -onset RCC. Screening for DNA repair defects may uncover underlying mechanisms of early-onset RCC and potentially lead to application of treatments targeting DNA repair vulnerabilities in these patients.

Read Full Article:
www.ncbi.nlm.nih.gov/pmc/articles/PMC10123997/

New Grants in Center Prevention and Control

The multidisciplinary Cancer Prevention and Control (CPC) program at Fox Chase Cancer Center focuses on the integration of basic and applied research in molecular biology, oncology, and the behavioral, social, and population sciences to reduce the burden of cancer. The overall goal of CPC is to reduce cancer morbidity and mortality by addressing cancer disparities and enhancing cancer prevention and control in populations at an increased risk for cancer, especially the underserved. In the past year, a few new grants were awarded to the CPC researchers. Congratulations!

SPEECH
Co-investigators: Grace Ma and Camille Ragin
Despite advances in the early detection and treatment of cancer, persistent disparities in cancer incidence and mortality remain across populations. The Synergistic Partnership for Enhancing Equity in Cancer Health (SPEECH), a large comprehensive research partnership targeting health disparities within the Philadelphia-NJ-NYC region, was recently renewed by the National Cancer Institute for additional 5 years. The SPEECH Partnership employs a multi-pronged strategy to combat health disparities, including conducting innovative research with cutting-edge technologies and building a stronger pipeline of diverse health professionals and researchers. Together, these efforts are making a significant impact on enhancing the health of all of our communities.

Grace Ma

Camille Ragin

BCFR (Breast Cancer Family Registry)
Principal investigator: Mary Daly
The BCFR Cohort is a globally unique resource for addressing important and unanswered clinical and population health questions about the development and biology of breast cancer and long-term outcomes for women affected by breast cancer.

Since its inception in 1995, the BCFR Cohort has recruited and followed by 6 sites in the U.S., Canada, and Australia 33,037 women and 6,992 men from 15,056 families. This grant was renewed by the National Cancer Institute for additional 5 years and will expand the Cohort through enrollment of young women with breast cancer diagnosed at age ≤45 years and their family members while oversampling underrepresented populations to increase racial, ethnic, and socioeconomic diversity.

Mary Daly

Training grant
Principal investigator: Carolyn Fang
This newly awarded training grant from the National Cancer Institute will support the professional development of the next generation of cancer control scientists. These scientists will be equipped to conduct innovative research in precision cancer control with diverse populations. Our trainees will learn how to utilize interdisciplinary approaches to address cancer risk factors and they will acquire critically important skills for developing effective interventions to reduce cancer morbidity and mortality.

Carolyn Fang

Pancreatic Surveillance for High-Risk Groups

By Kathleen Henderson, MSN, ANP-BC, Nurse Practitioner, Clinical Genetics

Average-risk individuals have an approximately 1-2% lifetime risk of pancreatic cancer. While pancreatic cancer accounts for 3% of new cancer cases, it is the 4th leading cause of cancer deaths. Risk factors for pancreatic cancer include tobacco use, obesity, type 2 diabetes, chronic pancreatitis, family history, and inherited genetic mutations.

Genetic mutations contribute to approximately 10% of cancers. All individuals with pancreatic adenocarcinoma are eligible for genetic testing. If these patients are unable to be tested, then their first-degree relatives (parents, siblings, children) may pursue genetic testing.

Inherited genetic mutations related to pancreatic cancer include (NCCN National Comprehensive Cancer Network guidelines):

- >15% risk with STK11, CDKN2A mutations
- 5-10% risk with ATM, BRCA2 mutations
- 2-5% risk with PALB2 mutation
- Up to 5% with BRCA1 mutation
- 1-6% with Lynch syndrome (MLH1, MSH2, MSH6, EPCAM, PMS2), depending on which gene is affected

While our common cancer screenings (mammogram and colonoscopy) apply to the general population, pancreatic surveillance is aimed towards high-risk individuals. It is best to perform this screening in a clinical trial at experienced high-volume centers. Individuals seeking this screening should understand the possibility of benign findings, financial responsibility, and uncertain benefit.

The **CAPS-5 trial (Cancer of the Pancreas Screening)** is sponsored by Johns Hopkins University, and started enrollment in January 2014 across 8 medical centers in the US (including PennMedicine at the Hospital of University of Pennsylvania). The goals of this trial are early detection of pancreatic cancer and long-term survival. Screening modalities include endoscopic ultrasound (EUS), MRI abdomen with contrast (MRCP), and tumor marker tests.

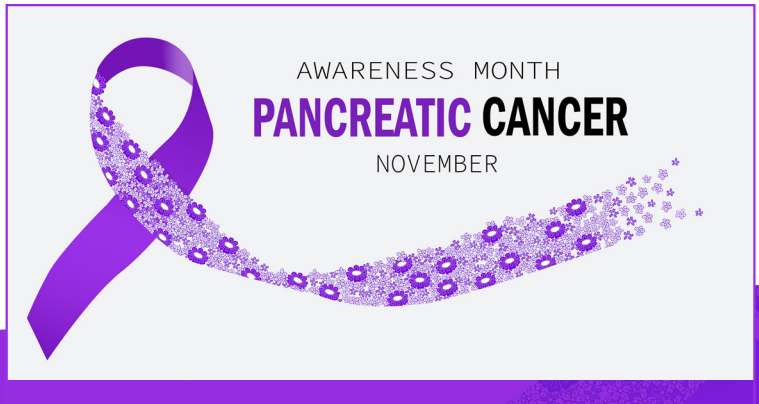
There are several patient cohorts that designate criteria and initiation of surveillance:

- STK11 mutation (Peutz-Jeghers syndrome): age 30 or older
- CDKN2A mutation: age 40 or older
- BRCA2, ATM, PALB2 mutations: age 50 or 10 years earlier than youngest relative with pancreatic cancer (whichever is earlier)
- BRCA1 mutation, Lynch syndrome: age 50 or 10 years earlier than youngest relative with pancreatic cancer, with at least 2 close relatives with pancreatic cancer
- Hereditary pancreatitis (PRSS1, PRSS2, CTRC): age 50 or 20 years since first pancreatitis attack (whichever is earlier)
- Family history of pancreatic cancer with no genetic mutation: age 55 or 10 years earlier than youngest relative, with at least 2 close relatives with pancreatic cancer, and have first-degree relationship with one relative.

The **PRECEDE Consortium (Pancreatic Cancer Early Detection)** is an observational study to assist research efforts in the early detection and prevention of pancreatic cancer. Criteria for high-risk individuals are similar to CAPS-5 trial with some variation. Participants between age 18-90 will submit a blood sample every 6-12 months with clinic visits. The study coordinator at Fox Chase is Sara Snell can be reached at 215-214-1588.

Individuals with an increased risk of pancreatic cancer can discuss screening options with a Fox Chase gastrointestinal physician specializing in this area: Dr David Loren, Dr Malorie Simons, or Dr Joseph Triggs.

In summary,
if you fit into a high-risk category as mentioned above, it is advised to avoid tobacco use, discuss screening options with a gastrointestinal specialist, and obtain annual fasting glucose and HbA1c labs to monitor for diabetes.



CHECKING IN ON CHEK2: UPDATES FOR LOW PENETRANCE CARRIERS

By Corinne Zrada and Chau Nguyen, genetic counselors

The CHEK2 gene is often classified as a "moderate risk cancer predisposition gene," and is traditionally associated with a higher than average population risk for breast and/or colon cancer. Currently, CHEK2 mutations carriers are quoted to have a lifetime risk of 20-40% for breast cancer and 5-10% for colon cancer.

Although CHEK2 is well established as a moderate risk gene, it is becoming more apparent that an individual's cancer risk related to a CHEK2 mutation can be influenced by the specific CHEK2 mutation an individual has, personal and/or family history of cancer. We are starting to learn that even among CHEK2 mutation carriers, some CHEK2 mutations can carry higher or lower risks for cancer compared to others.

The American College of Medical Genetics (ACMG) recently released an updated practice resource to help guide clinicians regarding management for individuals with CHEK2 mutations.

Two common CHEK2 variants -- p.Ile157Thr, also known as I157T, and p.Ser428Phe also known as S428F have earned the titles of "low penetrance," due to conflicting evidence from studies that these variants can be associated with a slightly increased cancer risk, (although much lower than other CHEK2 mutations), or none at all. This conflicting information has often left clinicians to wonder how to best manage patients with low penetrance CHEK2 mutations—should breast mammogram screening begin earlier for females? Should breast MRIs be added as routine care? Should early colonoscopy screening be standard?

In the latest ACMG practice resource, ACMG emphasizes that cancer risks associated with the I157T and S428F variants alone are not elevated enough to alter medical management in individuals without a family history of cancer.

For patients, this newest change symbolizes that for individuals who are found to carry the CHEK2 I157T or S428F variant but with no family history of cancer, cancer screening such as those for breast and/or colon cancer would be similar to that of the general population. For individuals with a CHEK2 I157T or S428F variant and a family history of cancer, cancer screenings may be individualized, based on personal and family history.

With this latest ACMG resource change, genetic counselors and genetic providers are moving towards more personalized cancer risk assessment. This more personalized assessment, similar to what ACMG concludes too, stresses the importance that clinical management for CHEK2 mutation carriers should be based on the specific CHEK2 mutation an individual was identified to carry, personal and/or family history of cancer, and other known genetic and environmental risk factors.

If you tested positive for a CHEK2 mutation, we encourage you to keep in contact periodically with your genetic provider for updates regarding cancer screening and management. If you have further questions, please free feel to reach out to the Department of Clinical Genetics at FCCC by calling 877-627-9684.

Chau Nguyen, MS, CGC

Corinne Zrada, MS, LCGC

Still Unsure What Exactly This Change Means for You?

Let's Walk Through Some Examples

Example 1: A 35-year-old woman with no personal history of cancer tested positive for the I157T low penetrance CHEK2 variant. Her mother has a history of breast cancer at age 58 and her maternal grandmother has a history of breast cancer at age 55.	**Example 2:** A 35-year-old woman with no personal history of cancer tested positive for the I157T low penetrance CHEK2 variant. She has no family history of breast cancer.
Clinical Screening Recommendations: Based on her family history of breast cancer and the presence of the CHEK2 variant, our RAP team may recommend she consider beginning breast screening earlier than the general population at age 35.	**Clinical Screening Recommendations:** Our RAP team would recommend general population screening for this woman (mammograms beginning at age 40) as the presence of the I157T variant alone is not enough to warrant management change in individuals with no family history of cancer.

What to know about breast density with Dr. Austin Williams

Austin D. Williams, MD, MSEd, Breast Surgical Oncologist

What does it mean to have dense breasts?
In order to understand what dense breasts means, it's important to understand what the breasts are composed of. Breasts are composed of two types of tissue: fatty tissue, and what we call fibroglandular tissue, or the milk ducts.

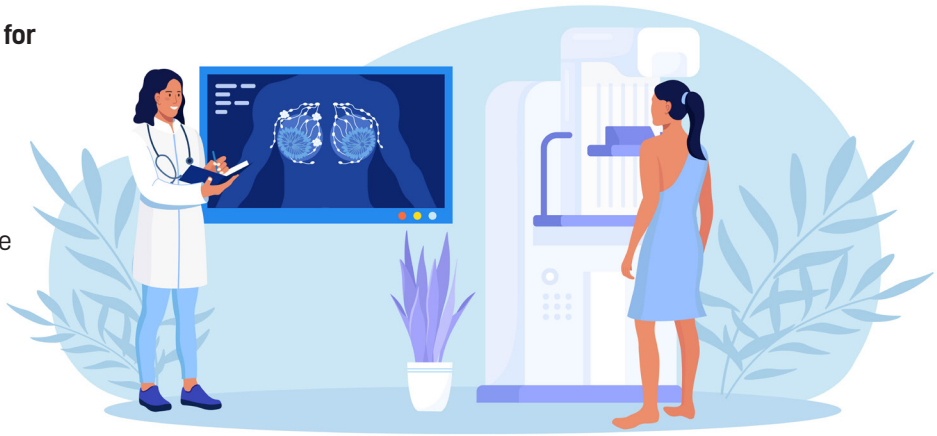
In dense breast there are relatively high amounts of fibroglandular tissue and low amounts of fatty breast tissue. Breast density is a proportion of fatty tissue versus fibroglandular tissue as seen on mammogram.

What factors influence breast density?
A known factor that influences one's breast density is age. As women age, their breast density decreases, and most of that is related to hormones and menopause. During the menstrual cycle and in premenopausal women, the fibroglandular tissue is more active, and after menopause, it becomes less active, therefore breasts become less dense.

Another factor that impacts breast density is BMI. Patients who have a higher BMI most of the time have more fatty tissue throughout their body, therefore their breasts are less dense, but that is not always the case.

I published a study a couple of years ago where we looked at patients who underwent bariatric (weight loss) surgery and found that if patients lose a lot of weight and fatty tissue is going away, you might expect breast density to increase. But we found that breast density actually decreased after bariatric surgery, and it's likely due to other reasons being related to biological mechanisms and hormones at play.

Is breast density associated with an increased risk for breast cancer?
What we know is that breast density is not a factor itself that is associated with an increased risk for developing breast cancer. Fibroglandular or dense tissue looks white on a ma mmogram, therefore it's hard to tell the difference between tumor and dense breast tissue, so a small tumor may be missed.

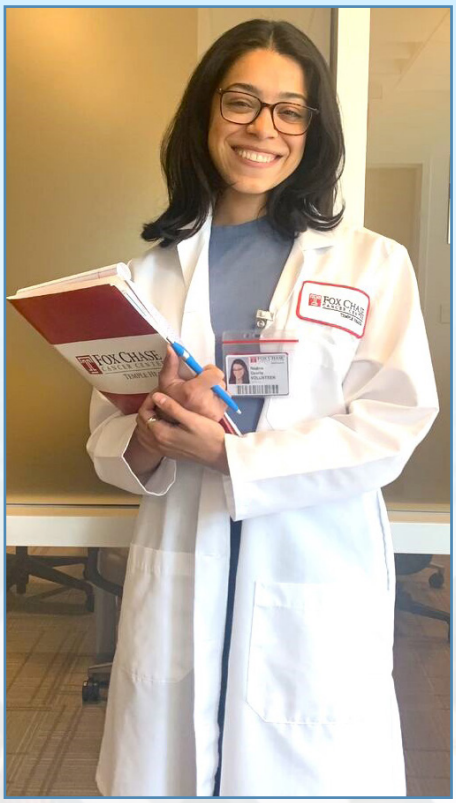


When should a woman be concerned about dense breast?
I don't necessarily know that they need to be concerned, meaning that not every patient with dense breast is going to develop breast cancer. When a patient undergoes a mammogram, there is a statement from the radiologist about patient's breast density. There are four categories ranging from very fatty to very dense. About 10% of women have very fatty breasts, about 10% of women have very dense breasts. And then 80% of patients find themselves somewhere in the middle.

If a patient is told that they are in that 10% with very dense breasts, those are the patients who really should be talking to their physicians about additional screening. It may include an ultrasound that is done at the same time as the mammogram and as part of the screening if a patient also has either family history or some other reason where their risk for developing breast cancer is substantially higher than that of the general public.

They may qualify for MRI screening as opposed to just mammogram and ultrasound, but not every woman with dense breasts should be undergoing MRI, and there are no actual national guidelines for screening in patients with dense breasts.

Summer Student in the Department of Clinical Genetics



My name is Nadine Osorio and I was born and raised in New York City. I'm currently a graduate student in the Integrated Program of Nutrition and Dietetics at Hunter College working toward achieving the Registered Dietitian credential. I had earned my bachelor's degree in public accounting but after working in the financial sector for a few years, I decided to pursue a career more aligned with my personal interests and values. Frustrated with the misinformation surrounding diets and food and becoming aware of the continuous increase in life-style related comorbidities, I desired to become educated in evidence-based nutritional therapies to help people who are struggling with managing their health. During my free time I enjoy cooking new recipes, listening to podcasts, and escaping the city to explore nature with friends.

This summer, through the Summer Cancer Research Institute program at Fox Chase, I've had the privilege to learn from Dr. Hall, a GI oncologist and Kara Stromberg, a Clinical Manager of Nutrition and Food Services, and her team of dietitians. I worked on a research project titled: "A Medically Tailored Meal Delivery Program to Improve Chemotherapy Tolerance in Patients with Colorectal Cancer: A Pilot Study."

They've brought me into their clinics, introduced me to their patients, and emphasized the importance of a multidisciplinary team to provide the highest quality of patient healthcare. These experiences, along with meeting members of the department of Clinical Genetics and assisting in participant recruitment for research, have solidified my interest to practice as a clinical dietitian to eventually specialize in oncology care.

Thank you to everyone who has guided me through this pivotal experience at Fox Chase Cancer Center.

HEALTHY RECIPE: Pumpkin Spice Energy Bites

Pumpkin, which is part of the winter squash family is filled with vitamin C, fiber and special phytochemicals called carotenoids, which are linked with protection from heart disease and cancer. Easy to prepare with no added sugar, plant-based energy bites are perfect for pre- or post-workout snacks, kids' (and grownups'!) lunchboxes and afternoon pick-me-ups with tea or coffee. Each bite is packed with protein, vitamins, minerals, fiber and phytochemicals to boost your nutrition.

Ingredients:

- 3/4 cup old-fashioned oats
- 2 Tbsp. hemp seeds
- 2 Tbsp. chia seeds
- 2 Tbsp. flax seeds
- 1/2 cup walnut pieces
- 1/4 cup pumpkin seeds
- 2 tsp. pumpkin pie spice blend
- 1/3 cup dried cranberries or raisins
- 1 cup canned or cooked pumpkin
- 10 small soft dates, pitted
- 1/3 cup creamy natural peanut butter
- 1 tsp. vanilla

Topping: 1/3 cup pumpkin seeds
Makes 28 servings (1 ball). Per serving: 90 calories, 5 g total fat (.5 g saturated fat, 0 g trans fat), 0 mg cholesterol, 10 g carbohydrates, 3 g protein, 2 g dietary fiber, 10 mg sodium, 6 g sugar, 0 g added sugar.

Directions:

1. Place oats, hemp, chia, flax, walnuts, ¼ cup pumpkin seeds, pumpkin pie spice and dried raisins in container of food processor. Process a few seconds, just until ingredients are finely ground.
2. Add pumpkin, dates, peanut butter and vanilla and process for a few minutes until smooth, pausing to scrape down sides as needed. Texture should be smooth, finely ground and sticky.
3. Pour mixture into bowl, cover and chill for about 1 hour.
4. Remove from refrigerator and form into small balls (makes 28 balls) with hands.
5. Place 1/3 cup pumpkin seeds in small dish and roll each ball in pumpkin seeds to coat.
6. Store in refrigerator in airtight container.

For more healthy recipes visit:
www.aicr.org/cancer-prevention/recipes/

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@fccc.edu

Mary Daly, MD, PhD
Director, Risk Assessment Program

Michael Hall, MD, MS
Chair, Department of Clinical Genetics

FOX CHASE CANCER CENTER AT BUCKINGHAM

The Department of Clinical Genetics is pleased to announce the expansion of our genetic counseling and high-risk clinical services at the Fox Chase Buckingham location, located at 2365 Heritage Center Drive, Furlong, PA 18925.

Starting November 6th, we will be offering two weekly genetic counseling and testing clinics: Mondays with Catherine Neumann, MS, LCGC and Wednesdays with Michelle McSweeny, MS, LCGC. We will also offer a high-risk breast and ovarian cancer clinic run by Kathleen Henderson, MSN, ANP-BC on the 1st Monday of each month for those eligible to participate.

To schedule an appointment, please call 877-627-9684.

Editors: **Yana Chertock, Nicole Ventriglia, and Deborah Grace**
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