

Prevention Matters

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When the Search for Answers Creates More Questions

By Kim Rainey, MS, MEd, LCGC, a Genetic Counselor

You may decide to have genetic testing to learn if you have an increased risk for cancer or to try to find a reason for your cancer diagnosis. Most cancers are due to a random series of events that damage our genes in critical places and are not due to an inherited risk.

In the past, when genetic testing was still a young science, we looked at a few genes at a time to see if there were any errors in the genetic code, called "mutations," that increased the risk for certain cancers. These errors were inherited from a parent and could be passed on to the next generation. Now that gene sequencing is fast and much less expensive, we tend to cast a wide net and look at multiple genes through "gene panels". We sometimes find an error in a gene and we are not entirely sure about the level of risk for certain cancers. There may not be established screening recommendations for carriers of certain gene mutations. For some people, this uncertainty can lead to more worry after genetic testing.

Another major cause for uncertainty that comes with genetic testing is the finding of a "Variant of Uncertain Significance" or a "VUS". Since we are still learning about many of the genes, we often get a test result which is not "positive" or "negative". The lab must be able to state with a high level of confidence, that if your genetic code is different from the expected code, that difference leads to an increased cancer risk. If they do not have enough information to state that with confidence, they will classify the genetic variant as a VUS and they will continue to study it and gather more information until they can make a decision. Your test result will be considered "inconclusive", however it is treated the same as a "negative" test result. A VUS is innocent until proven guilty.

The reason we treat a VUS the same as a negative result, is because the majority of VUSs are reclassified as "negative" once the laboratory gathers enough evidence. When the test result is "negative" or

"inconclusive", we use your family history of cancer to guide the recommendations for your cancer screening. We don't recommend genetic testing to family members for a VUS and we don't change your medical care when you get a VUS on your genetic testing.



The reason we get so many VUSs in our genetic testing is because genes have a fair amount of "wiggle room" built into the genetic code. That wiggle room is important for evolution. Nature can select one slight variation over another if there is a survival advantage. Genes can have a slightly different code than what is expected and still work perfectly well to protect us from cancer. So that is the challenge for genetic testing labs, they must decide which variations work just fine and which variations come with an increased cancer risk.

It can take months or years for the labs to gather enough information to come to their final decision. Your genetic counselor will be notified by the lab when the VUS is reclassified and you will be contacted with the updated report. If your genetic test report has a VUS, it is important to provide your updated contact information so you can be notified of any updates.

So, if you are thinking about having genetic testing, do some soul searching about how you will handle the possibility of an uncertain result. Will it keep you up at night or will you be able to manage it? If you already had genetic testing and you are waiting for your VUS to be reclassified, feel free to check in with your genetic counselor from time to time to see if there are any updates.



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Summer Students in the Department of Clinical Genetics

Kiera Murphy BRIP1 gene

Kiera Murphy is a junior at The College of New Jersey. She is currently studying biology on a pre-med track as a part of the Honors Program. During this past school year, she participated in research that measured hypothetical alcohol abuse in humans as well as the neurological processes behind reward learning and decision making. This summer, she was given the opportunity to complete research with Dr. Michael Hall in the Department of Clinical Genetics at Fox Chase Cancer Center. Through collaboration with Dr. Hall and Michelle Savage, a genetic counselor, Kiera explored the BRIP1 gene: a gene that is mostly known to be an ovarian cancer risk gene, yet studies suggest that it may have other cancer risks.

The BRIP1 gene is one of nineteen genes involved in the Fanconi Anemia (FA) pathway, a pathway that works to repair DNA lesions. It is currently known that if a woman has a pathogenic variant (a harmful mutation) in the BRIP1 gene, she is at a 5-10% increased risk of developing ovarian cancer. Variants in BRIP1 have also been seen in patients with prostate, breast, and colorectal cancer, yet the link remains unclear.

To further explore the cancer risk associated with BRIP1, specifically related to colorectal cancer, Kiera obtained 49 families with known BRIP1 variants

(determined through commercial lab testing), including both pathogenic variants and variants of uncertain significance (VUS). The sample was representative, containing men and women from several ethnicities and ages ranging from 25-84 (average age of 53 years).



Through examining the lab test results, reviewing family histories of cancer diagnoses, and using online algorithms to predict the disruptiveness of each variant, our data suggests that families with a BRIP1 variant have characteristics of a hereditary gastrointestinal cancer syndrome.

While this research has been informative, the sample size was limited. To further study this, a larger sample is needed in order to reclassify VUS cases as either harmful or benign. Although this will take time, it is important to determine the genes that lead to an increased risk of GI cancer in order to promote proactive behaviors, such as genetic testing or preventative screening in families at risk.

Allaina Brock

Allaina Brock joined the Department of Clinical Genetics as a summer student. She worked closely with Dr. Michael Hall to create a database of the many families with Lynch Syndrome in the Risk Assessment Program. Allaina is excited that she will be able to continue her work throughout the fall as she attends Bryn Athyn College. She is interested in statistics, and this summer, participated in a biostatistics internship where she learned many statistical programs. She hopes to continue her research at Fox Chase. Allaina is also very interested in genetic counseling. She was able to shadow the genetic counselors at Fox Chase and join weekly department meetings. She loved meeting with patients and learning about genetics. Her goal is to enter a Genetic Counseling program when she graduates in 2021.



WELCOME ABOARD: Natasha Beauchmin

The Department of Clinical Genetics, Risk Assessment Program is pleased to welcome our new Intake Coordinator Natasha. Natasha's primary goal will be to work with patients referred to the Risk Assessment Program to explain the components of our program, collect personal and family history information and schedule patients for Cancer Risk Counseling and Genetic Testing with our team of Genetic Counselors. Natasha previously worked in the Ambulatory Care Department as a Medical Assistant for the Endocrinology Department. We are happy to have her on board and look forward to her having a rewarding experience working with our dynamic team.



Collecting and Sharing Your Cancer Family History

Your family health history provides a powerful tool for understanding your risk of developing certain diseases. When meeting with a cancer genetic counselor, your family history of cancer helps guide the counselor to choose the best genetic test or panel for you and your family. These test results can impact you and your extended family if a genetic mutation is found.

Your family history of cancer can also help your doctor determine whether you may need more intensive follow-up care, even if you do not need genetic testing. Here are some tips that will help you effectively gather your family's health history:

1. Start with your parents and any living grandparents. Often, older relatives can serve as a "family historian". If you are adopted, it is important to know that only your biological relatives should be taken into consideration. Talk to your adoption agency to locate any possible family records.

Ask specific questions:

- What was the type of cancer(s)?
- What was the age at diagnosis?
- What side of the family - mother's (maternal) or father's (paternal)?
- What is the family ethnicity (some ethnicities, such as the Ashkenazi Jewish population, are at greater risk for certain cancers)?
- What are the results of any cancer-related genetic testing?

2. Reach out to more distant relatives, including cousins, aunts, and uncles on both sides of the family.
3. Use social media, such as Facebook or Twitter, and social events such as reunions or weddings, to connect with your relatives.
4. Some relatives may want to keep their personal health history private. It is important to respect their wishes and not push too hard for their information.
5. Write down any information you learn and share it with your doctor, genetic counselor, and family members, including your children and siblings.

For more information visit Cancer.Net:
<https://www.cancer.net/navigating-cancer-care/cancer-basics/genetics/collecting-your-family%E2%80%99s-cancer-history>

Decision-making in Women with Ovarian Cancer Risk

Currently there is little information about how women with a hereditary risk for ovarian cancer make decisions when choosing prevention strategies for their associated risks.

The more doctors and counselors learn about cancer risk associated with each specific genetic mutation, they will be able to give each patient personalized information about their risk. It is important that clinicians have the information to develop counseling models that work for each patient's preferences for cancer risk reduction.

Dr. Mary Daly is working with Dana Farber Cancer Center on a new study called "Assessing Personal Thresholds for Risk to Undergo Risk-Reducing Surgery". The study is looking to determine women's pre- genetic test preferences for risk-reducing surgery to remove their ovaries and/or fallopian tubes vs no surgery. Participants will complete an online survey that provides education as well as a questionnaire. Education provides participants



a chance to learn more about potential side effects of risk reducing surgery before choosing which option might be right for them. After receiving genetic test results, participants will be asked to complete the survey again to see if their preferences have changed.

NOVEMBER IS PANCREATIC CANCER AWARENESS MONTH

PURPLESTRIDE PHILADELPHIA 2019

Pancreatic Cancer Action Network 5K Run & Family-Friendly Walk

Saturday, November 2, 2019 8:00am

Memorial Hall/Please Touch Museum, Philadelphia, PA 19131

<https://www.foxchase.org/events/purplestride-philadelphia-2019>

IMPORTANCE OF GENETIC TESTING IN PANCREATIC CANCER

Michael J Hall, MD, MS, Chair of the Department of Clinical Genetics at Fox Chase Cancer Center, gave several interviews at the 2019 ASCO Annual Meeting about the importance of genetic testing in pancreatic cancer related to his participation on the steering committee of the POLO trial (olaparib maintenance therapy in pancreatic cancer).

Mutations in pancreatic cancer are common and can be found in 10-15% of all pancreatic cancer patients. Information about clinically relevant mutations can be very important not only for patients but also for their family members.

Dr. Hall explained that genetic testing today is widely available, inexpensive, and testing for pancreatic patients is recommended in the NCCN (National Comprehensive Cancer Network) guidelines.



Michael Hall, MD, MS

He discussed some barriers to genetic testing. Some physicians are reluctant to discuss genetic testing because often patients are too sick to focus on anything but their illness. Also, people are still afraid of germline testing; in particular they're concerned about privacy, and worried about family members who might be upset if they find out about a mutation that could lead to cancer.

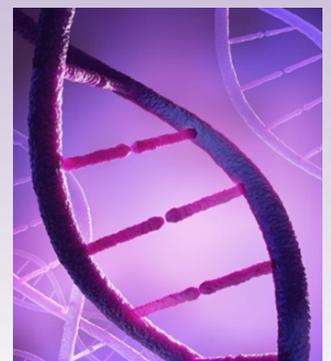
Dr. Hall suggests that all providers talk to patients about how testing will benefit their care and family.

The POLO Trial in Metastatic Pancreatic Cancer

New data from the phase III POLO international trial was presented at the 2019 ASCO Annual Meeting.

The randomized phase III POLO trial found that treatment with the drug olaparib significantly delayed the progression of metastatic pancreatic cancer in patients with germline BRCA gene mutations compared with placebo.

Olaparib (LYNPARZA) is a PARP inhibitor, a type of targeted therapy that blocks the repair of damaged DNA in cancer cells, making them unable to survive and divide. The primary endpoint of this study was progression-free survival, which was 7.4 months in the olaparib group versus 3.8 months in the placebo group. Olaparib was well tolerated, and there was no difference in quality of life between those taking olaparib and placebo.



Dr. Michael Hall, one of the investigators of the POLO trial, explains the idea behind this trial.

“Pancreas cancer is one of the most dismal tumors in all of oncology. What we have discovered over the years is that the only option to control disease once it spreads outside of the pancreas, which is 80% of patients when they are diagnosed, is to use multi-agent chemotherapies that are very toxic for patients. The challenge behind that is you’re offering someone who is already very sick from the disease toxic chemotherapy to be able to extend their lives another 6-8 months. That’s not necessarily something that’s attractive to a patient. They want extended disease-free survival and quality of life; they want to have both.

The idea behind this was that there were some preliminary data several years ago that showed that in patients with pancreas tumors that have a germline BRCA mutation, and at that point we knew the range was maybe 5% to 15%, we knew that those tumors responded differently than the other pancreas tumors.

They seemed to be especially sensitive to platinum-based agents. Talia Golan, MD, who is the senior author on the study, published a study in the Journal of Clinical Oncology showing that platinum agents were particularly good in this subgroup of patients with pancreas cancer.

Over time, we understood it was the BRCA deficiency that was driving this sensitivity to therapy, so when the PARP inhibitor class of agents was developed, naturally this became something of interest. I think a lot of people first looked at pancreas cancer and said there is no way an oral agent will ever be able to control this disease. That was a real gamble and it paid off. The trial was born of that.”

For more information about the trial:
<https://www.ascopost.com/News/60105> or
<https://clinicaltrials.gov/>

REC Patient Education Session: Updates in BRCA-Related Hereditary Breast and Ovarian Cancer

Speaker: Catie Neumann, Genetic Counselor
Tuesday, January 21, 2020 1:00pm to 2:00pm
Location: Fox Chase Cancer Center Resource and Education Center
1st Floor, Young Pavilion
To register, please call the REC at 215-214-1618



Breast Cancer Family Registry



The Breast Cancer Family Registry (BCFR) is an international resource of multi-generational families, data, and biospecimens established for

research on breast cancer. Over 30,000 women and men from nearly 12,000 families from the United States, Canada, and Australia have dedicated their time to participate in the BCFR. The BCFR resource has been used and continues to be used by breast cancer researchers around the world in order to find new ways to prevent, diagnose, and treat cancer.

Over 300 scientific articles have been published by researchers using the BCFR data with major breakthroughs in the following areas:

- Discovered hundreds of genetic variants that help explain some of the family clustering of breast cancer
- Provided more accurate risk estimates for use in clinical risk assessment
- Found other ways BRCA and other breast cancer genes affect breast cancer risk, including epigenetics

Fox Chase Cancer Center is one of the six international sites that make up the Breast Cancer Family Registry. It was established in 1995 and we are still going strong in 2019.

We have recruited over 2,800 participants to this study at Fox Chase!

This year we will be sending out a questionnaire to our current participants, as well as recruiting the next generation to our study. We will soon be looking to recruit the daughters of our current BCFR participants ages 18-40.

We appreciate your continued efforts to help with our research!

Please visit us at: <http://www.bcfamilyregistry.org/>



DIET AND PROSTATE CANCER RISK

A recently published article titled “Diet assessment among men undergoing genetic counseling and genetic testing for inherited prostate cancer: Exploring a teachable moment to support diet intervention”, discussed healthy lifestyle promotion and cancer prevention for men with prostate cancer and men at high risk for prostate cancer.

Our Prostate Risk Assessment Program (PRAP) team, led by Dr. Elias Obeid, collaborated with Dr. Veda Giri at Thomas Jefferson University on the Genetic Evaluation of Men Study (GEM). The study provided a multigene genetic testing panel as well as an education PowerPoint which explained genetic testing, possible results, and how testing would be valuable to each participant. Men with prostate cancer (PCA) or at high risk for prostate cancer were recruited at Fox Chase and Thomas Jefferson University. Each man completed several questionnaires as part of this study.



Participants completed a food frequency questionnaire. The questionnaire asked about number of servings consumed per day or per week of fruits, vegetables, red meat, seafood, processed meat and foods high in saturated fat. Researchers used adherence to the USDA recommendations and assessed each participant by PCA status and aggressiveness, family history, and body mass index (BMI). GEM participants reported consuming less fruit, less vegetables, less seafood, more processed meats and more foods high in saturated fat than recommended by the USDA.

Many of the men were either overweight (45.1%) or obese (37.2%) by the Centers for Disease Control (CDC) BMI classification. Obesity is associated with the development of aggressive PCA. Published data suggest that eating fruits, vegetables, dietary fiber and omega-3 fatty acids may help prevent developing PCA and slow cancer progression of men with PCA.

Genetic counseling sessions may provide an opportunity to discuss diet and obesity for men with prostate cancer.

Read the article: <https://onlinelibrary.wiley.com/doi/epdf/10.1002/pros.23783>

OUR GUT – HOME FOR MICROBES

Our bowels are home to trillions of bacteria called microbes. Recent studies have shown that some of the microbes in our bowel can be important for maintaining bowel health while others may influence all aspects of health, from immunity and anxiety to chronic disease, including cancer and diabetes. Some bacteria fight inflammation, while others promote it. A balance of these two types of bacteria is key for the body’s well-being.

Many factors play a role in the bacterial makeup in our gut, such as the food we eat, the environment in which we grow up, and the medications we take.

Doctors recommend maintaining a healthy gut by following a balanced diet, staying hydrated, exercising regularly and getting a good night’s sleep.

Many commercial dietary supplements claim to improve gut health and introduce good bacteria. However, we still lack research data on the benefits of probiotic pills and capsules. The supplement industry is not well regulated,

and there is no guarantee that what’s in the bottle matches what’s on the label. Instead of pills, doctors recommend getting good bacteria from fermented foods* – like probiotic yogurt, kefir, sauerkraut, kimchi, kombucha, miso, and tempeh.



HEALTHY RECIPE

Moroccan Seven Vegetable Tagine

Tagines are flavorful stews named for the pot they're cooked in. But you don't need a special pot for this adaptation -- a large Dutch oven will do the trick just fine. This recipe features a simple combination of fall vegetables, chickpeas, herbs and spices. Butternut and other winter squash are packed with vitamin C, fiber and cancer-preventive carotenoids. Aromatic spices like turmeric are being studied for their ability to suppress inflammation.

Ingredients:

- 2 white turnips, peeled and quartered
- 1 cup sliced carrots, in 3/4-inch slices
- 1 cup finely chopped onion
- 1½ tsp. ground cumin
- 1 tsp. ground sweet paprika
- 1/2 tsp. ground ginger
- 1/2 tsp. ground turmeric
- Pinch of cayenne pepper
- 1½ cups reduced-sodium vegetable broth, divided
- 2½ cups butternut squash, in 1-inch cubes
- 1 cup chopped zucchini, in 3/4-inch pieces
- 1/4 lb. string beans, trimmed and cut in 1½-inch lengths
- 1 (15 oz.) can no salt added chickpeas, drained
- 3/4 tsp. salt
- Freshly ground black pepper
- 3 plum tomatoes, cut crosswise into 3/4-inch slices
- 1/4 cup chopped cilantro
- 1/4 cup chopped flat-leaf (Italian) parsley

Directions:

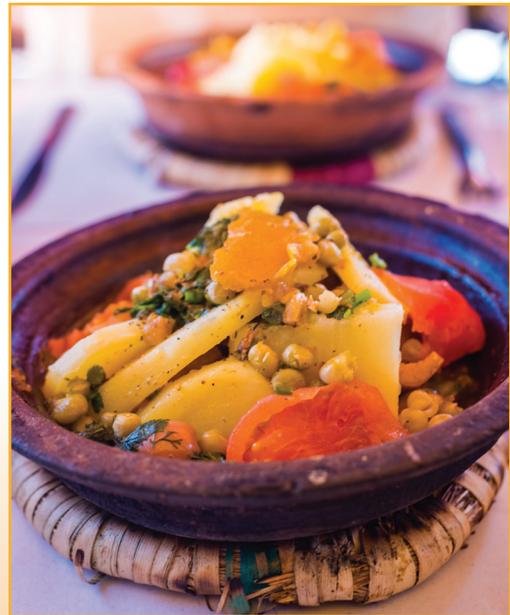
In medium Dutch oven, combine turnips, carrots, onion, cumin, paprika, ginger, turmeric and cayenne. Pour in 1 cup broth. Cover and simmer over medium heat for 10 minutes.

Add butternut squash, zucchini, string beans, chickpeas and remaining broth. Add salt and 3-4 grinds of pepper. Cover and cook until vegetables are tender, 20 minutes. Arrange tomato slices on top of the vegetables, cover, and cook until tomatoes are just soft, 5 minutes. Add cilantro and parsley and let tagine sit, covered, for 10 minutes to allow flavors to meld. Serve hot, directly from pot. This dish improves when reheated so, if desired, cool, cover, and refrigerate for up to 2 days. Reheat, covered, over medium heat.

Makes 6 Servings (8 cups)

Per approx. 1½ cup serving: 149 calories, 2 g total fat (<1 g saturated fat), 30 g carbohydrate, 7 g protein, 8 g dietary fiber, 485 mg sodium.

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***Fermentation** is a process that's used to produce some of our favorite foods and beverages — things like wine, beer, breads, cheese, chocolate, coffee and yogurt. Eating fermented (or "cultured") foods is the most convenient way to obtain a daily dose of beneficial probiotic bacteria. When food is fermented, it's left to steep until the sugars and carbs that are naturally in the food interact with bacteria, yeast and microbes to change the chemical structure of the food. The fermentation of foods, such as milk and vegetables, is also a great way to preserve them for a longer period of time and make their nutrients more absorbable.



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

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SATURDAY, OCTOBER 26, 2019

Light the Night 2019
The Leukemia & Lymphoma Society's Light the Night Walk
Family Fun Zone & Fireworks
4:30pm to 8:30pm
Philadelphia Museum of Art, 2600 Benjamin Franklin Pkwy,
Philadelphia, PA 19130

THURSDAY, NOVEMBER 7, 2019

Together Facing Pancreatic Cancer (free event)
5:30pm to 8:00pm
Dinner will be served
Fox Chase Cancer Center Cafeteria- Center Building
333 Cottman Avenue, Philadelphia, PA 19111

WEDNESDAY, DECEMBER 11, 2019

Tree of Life Celebration
A special program to honor those touched by cancer
5:30pm to 7:00pm
Fox Chase Cancer Center Cafeteria, Philadelphia, PA
This event is free and open to the public.

To register, please visit foxchase.org or call 215-728-2745

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