Genetic Testing May Give Answers, but May Also Leave Questions
by Andrea Forman, MS, LCGC; Mary B. Daly, MD, PhD, FACP

Genetic testing and cancer care have a complicated relationship. There are a few key points that a patient should know prior to undergoing genetic testing of any kind. It is important to understand that there are different types of genetic testing that might be offered, multiple results are possible, and available treatment options may be limited.

- **Tumor genetic testing** looks for genetic changes in a person’s cancer or tumor which can help a doctor decide if one treatment might work better than another. These genetic changes are usually present only in the tumor and do not affect future cancer risk or cancer risks of family members.

- **Hereditary, or germline, genetic testing** looks for DNA changes in a blood or saliva sample to tell the patient if they were born with, or inherited, a genetic change that increases their chances of developing cancer at some point in their life. Sometimes there is an increased risk for more than one type of cancer, and these types of genetic changes can be passed from generation to generation.

Once you know what type of test you are being offered, ask your doctor about the possible results and what you would do with that information.

[+] If a person tests positive for a hereditary genetic risk, it might change their recommendations for surgery in order to reduce the risk of developing a new cancer in the future or they may now be a candidate for a specific type of chemotherapy. Knowing that a person has an increased risk to develop cancer can help a patient pursue more careful cancer screening or risk reducing options. Sometimes, however, a positive result will not change anything that is already planned for treatment and follow up. A positive hereditary result can also cause worry and anxiety, which may lead someone to question why they did the test in the first place.

[ - ] A negative genetic result can be very reassuring in some ways, but it does not guarantee that a new cancer will never happen. Personal and family history may still support careful screening and follow up care. Make sure an accurate family history is reviewed when looking for inherited cancer risk.

[ ? ] The most frustrating result of all may be the “variant of uncertain significance” (VUS). Human DNA is full of genetic variations that do not cause disease. Sometimes a test finds a genetic change and we do not yet know if this is a normal human variant, or a change that increases cancer risk. These results are, indeed, “uncertain.” However, uncertain results should not affect medical care. With time and research, uncertain results will be reclassified as either benign (it does not affect cancer risk) or pathogenic (cancer risk is increased). When we look at VUS results that have been reclassified in the past, we find that the majority are benign and do not increase cancer risk.

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The Philadelphia Breast Cancer Family Registry (BCFR) has been established as a resource for future studies on genetics and diseases. Fox Chase and other research centers are collecting medical history, family history, lifestyle information, and biospecimens from many families that have a history of cancer. The data and specimens provide an ongoing source of valuable information for researchers who are studying ways to prevent, diagnose, and treat cancer.

The BCFR has a new pilot study for daughters of our participants. The pilot study aims to test the feasibility of recruiting younger women to participate in the Registry. The ultimate goal is to create a resource for future research on the biological factors and exposures experienced by women ages 18-40 that may be related to a future risk for breast cancer.

www.bcfamilyregistry.org

On September 28 - October 1, 2016 our genetic counselors attended the 35th Annual Education Conference in Seattle, Washington

The Cancer Risk Education and Wellness (CREW) study about the importance of discussing lifestyle risk factors in cancer genetic counseling was presented as a poster at the conference by Andrea Forman, a senior genetic counselor at Fox Chase and Victoria Dickens, a genetic counseling student at Arcadia University.

The purpose of the study was to discover genetic counselors’ and patients’ feelings about discussing lifestyle risk factors within a cancer genetic counseling session. 298 Risk Assessment Program (RAP) patients and 204 genetic counselors completed the online survey. At least 81% of patients rated every lifestyle factor (smoking, alcohol use, diet, obesity, and exercise) as very or extremely important to discuss in genetic counseling. Genetic counselors reported limited time, expertise, and scope of practice concerns as barriers for discussing these topics with patients during genetic counseling.

The survey results will help to guide the development of the CREW tool. Future studies will focus on the design of this tool as well as how best to incorporate this tool into genetic counseling sessions.

We would like to give a big THANK YOU to all the RAP participants who completed the CREW survey and contributed to this study.

Breast Cancer Family Registry Pilot Study

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Tumor Genetics May Have Critical Impact for Treatment Options

Dr. Michael Hall, Director of Gastrointestinal Risk Assessment at Fox Chase Cancer Center, was a faculty member at the 2017 Gastrointestinal Symposium on January 19-21 in San Francisco, CA. Dr. Hall was a guest speaker for the Genetic Testing in Colorectal Cancer session. His lecture was titled, “Emerging technologies for genetic testing.”

Dr. Hall emphasized the importance of genetics in oncology and the growing area of genomic tumor testing. He said that oncologists initially think about surgery and chemotherapy as the “big weapons” to fight cancer. However, Dr. Hall believes oncologists must all learn about the importance of tumor genomics in treating and preventing cancer. In some cases, it may be critical to have their patients see a genetic counselor or doctor who specializes in genetics before making a treatment decision, because decision making could be changed based on the genetic and tumor test results. Tumor genomics can also open new doors to treatment for some patients, and in some cases may suggest possible cancer risks for family members.
A NEW PHASE 3 CLINICAL TRIAL FOR COLORECTAL CANCER

A phase 3 clinical trial for colorectal cancer patients comparing a research study drug with standard chemotherapy drugs is being led by Michael Hall, MD, MS, who specializes in Gastrointestinal Cancers and Cancer Genetics. The study is sponsored by Merck Sharp & Dohme Corp.

The trial uses pembrolizumab, which is an investigational immunotherapy drug that targets a protein called PD-1 found on some cells of the immune system. Pembrolizumab blocks the interaction of PD-1 with another protein called PD-L1, sometimes found on tumor cells. Blocking this interaction may help the immune system recognize tumors and attack them. The purpose of the clinical trial is to find out if pembrolizumab can improve disease and increase progression free survival better than the standard chemotherapy doctors usually give for this disease.

About 270 patients with stage IV Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) colorectal cancer will participate in this study.

For more information visit:  www.foxchase.org/clinical-care/search-clinical-trials

March is Kidney Cancer Awareness Month

INVESTIGATING NOVEL GENETIC RISK FACTORS FOR HEREDITARY RENAL CANCER
by Sanjeevani Arora, PhD, Research Associate, Molecular Therapeutics Program and Cancer Prevention and Control Program

Renal cell cancer (RCC) is among the more commonly diagnosed cancers in both men and women. Hereditary renal cancers make up approximately 3-5% of renal cell cancers. Some genetic mutations have been identified in families and have been associated with high levels of inherited risk. The seven known renal cancer genes - VHL, MET, FLCN, TSC1, TSC2, FH and SDH - are involved in cellular metabolism which is a chain of chemical reactions that maintain life. Other genes are involved in DNA damage response and repair; these genes protect our genome against genotoxic insults, which can cause mutations and cancer.

However, despite this progress, the majority of hereditary renal cancer cases remain genetically undefined. It is likely that there are other genes that present low-to-moderate risk, fall under similar pathways like the high-risk genes and contribute towards inherited genetic risk. In a new study at Fox Chase Cancer Center, Dr. Sanjeevani Arora with Dr. Mary Daly, Director of Risk Assessment Program, and other researchers have examined the genetic basis of hereditary renal cell cancer of genetically undefined cases.

The study has analyzed 25 early-onset familial RCC cancer cases from Risk Assessment Program families utilizing Next-Generation Sequencing technology, to study genetic changes. The investigators studied the entire network of genes that are involved in cellular metabolism, DNA damage response and repair, and genes known to be involved in renal disease. Through sequencing, novel or rare germline variants (inherited genetic alterations) were identified and functional studies are being performed to confirm genomic findings. Further studies could explain novel molecular factors, which may help predict risk within families and improve screening and diagnosis.
Have you hit the big 5-0? It’s time to get tested!

Do you know the symptoms of colorectal cancer?
You should see your health care provider if you have any of the following:

- A change in bowel habits, such as diarrhea, constipation that lasts for more than a few days
- A feeling that you need to have a bowel movement that’s not relieved when you go
- Rectal bleeding
- Blood in your stool
- Cramping or belly pain
- Weakness and tiredness
- Unintended weight loss

» If you are a man or a woman age 50 or older, talk to a doctor about getting tested for colon cancer, even if you don’t have any symptoms.
» If you have a family history of colon cancer or polyps, you may need to get tested earlier than age 50. Discuss your family history with a doctor.
» Colon cancer can be prevented with regular testing. There are a number of tests available. Talk to a doctor or nurse about the test that’s right for you.

<table>
<thead>
<tr>
<th>Test</th>
<th>How test is performed</th>
<th>How often</th>
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<tbody>
<tr>
<td><strong>STOOL TESTS</strong></td>
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<tr>
<td>Guaiac-based fecal occult blood test (gFOBT) and Fecal immunochemical test (FIT)</td>
<td>Samples of stool (poop) are checked for blood, which might be a sign of a polyp or cancer. People take these tests at home with a kit they get from their doctor’s office, along with instructions.</td>
<td>Once a year</td>
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<tr>
<td><strong>SCREENING TESTS</strong></td>
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<tr>
<td>Sigmoidoscopy</td>
<td>The doctor puts a flexible, lighted tube into the rectum and lower colon to look for polyps and cancer. Bowel prep may be needed to clean out your colon before this test. Most people do not need to be sedated during this test.</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>The doctor puts a longer, flexible tube into the rectum to look at the entire colon and rectum. If polyps are found, they may be removed during the test. You’ll need to clean out your colon with strong laxatives. Most people are sedated during the test.</td>
<td>Every 10 years</td>
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<tr>
<td>Double-contrast barium enema</td>
<td>This is an x-ray test of the colon and rectum. It requires a bowel prep, but no sedation.</td>
<td>Every 5 years</td>
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<tr>
<td>CT colonography (virtual colonoscopy)</td>
<td>This is a type of CT scan of the colon and rectum. It requires a bowel prep, but no sedation.</td>
<td>Every 5 years</td>
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Source: American Cancer Society

For more information, visit cancer.org/colon
Study suggests that all men with metastatic prostate cancer should be tested for inherited mutations

In a new study published in the New England Journal of Medicine (NEJM), researchers from multiple institutions in the United States and United Kingdom performed genetic testing on 692 metastatic prostate cancer patients. The goal was to identify occurrence of mutations in the patients’ DNA repair genes. These genes, which include the BRCA genes, correct errors that arise when cells duplicate their DNA before dividing.

Researchers found mutations in 11.8% of men with metastatic disease. Mutations were found in 16 different genes; the most common was in the BRCA2 gene. This mutation is known to increase the risk for breast, ovarian and pancreatic cancer in addition to prostate cancer. Other genes found in this group were ATM, CHEK2, BRCA1, RAD51D and PALB2.

This information was compared with the frequency of gene mutations among 499 men with localized prostate cancer. Only 4.6% of men in this group were found to have mutations in DNA repair genes. Among 53,105 individuals without a known cancer diagnosis, mutations were identified in 2.7% of men.

The results suggest that all men with metastatic prostate cancer, regardless of age or family history, be tested for inherited mutations in genes that are responsible for DNA repair.

Screening for these mutations may provide treatment options for men, such as PARP-inhibitors (Olaparib) and certain kinds of chemotherapy. In addition, it would help alert family members to seek genetic counseling to determine their own cancer risks.

Read the original article at: www.nejm.org/doi/full/10.1056/nejmoa1603144

June 12-18, 2017 - National Men’s Health Week
www.cdc.gov/men/nmhw/

A human papillomavirus (HPV) vaccine is recommended routinely for boys at 11 or 12 years of age to prevent anal cancer and genital warts. The vaccine also is recommended for all teenage boys and men through age 21, any man who has sex with men through age 26, and men with compromised immune systems (including HIV) through age 26, if they did not receive all three doses of the vaccine when they were younger.
May 31, 2017 - World No-Tobacco Day

TOBACCO TREATMENT PROGRAM AT FOX CHASE:

- One-on-one counseling with our trained specialist
- Group sessions to provide support
- Medication to help calm cravings

To make an appointment please call:
888-FOX-CHASE or visit
FoxChase.org/TobaccoTreatment

May is Skin Cancer Awareness Month
Protect Your Skin from Sun Damage

According to the American Cancer Society (ACS), skin cancer is the most common cancer in the United States. There are three main types of skin cancer: basal cell, squamous cell, and melanoma. Basal cell and squamous cell develop on sun-exposed areas of the skin like the face, ears, neck, and lips; it is rare for them to spread to other parts of the body and become life-threatening. Melanoma, on the other hand, is much more dangerous and can develop anywhere on the body, even in places not normally exposed to the sun.

Consider these easy tips to protect your skin:

- Use sunscreen with an SPF of 30 or higher every day. Reapply every two hours and after swimming or exercising. Use sunscreen even on cloudy days.
- Cover up with tightly-woven clothing and a broad-brimmed hat. Avoid straw hats that let sunlight through.
- Seek shade, especially midday (between 10 AM and 4 PM) when the sun’s rays are strongest.
- Avoid tanning. According to the Centers for Disease Control and Prevention (CDC), tanning beds increase a person’s risk of getting skin cancer. Both indoor and outdoor tanning are dangerous.

“The great news is that both basal cell and squamous cell skin cancers and melanoma are often curable when found and treated early,” says Fox Chase surgical oncologist Jeffrey M. Farma, MD, FACS. “Everyone is subject to the potential adverse effects of sun overexposure. The key is to play it safe by avoiding prolonged exposure and practicing sun safety.”

For more information visit National Cancer Institute (NCI) website:
**Powerhouse Quinoa Bowl**

If you’re looking to mix up your grains, look no further than quinoa. This seed can be cooked and used in place of grains and contains all essential amino acids, making it a good source of protein. Pairing with broccoli and cauliflower gives this bowl a fresh crunch and adds vitamin C, folate and cancer protective glucosinolates. These compounds may decrease inflammation, a risk factor for cancer.

### Quinoa with Cauliflower and Broccoli

- 1 Tbsp. extra virgin olive oil, divided
- 2 cups cauliflower florets
- 2 cups broccoli florets
- 1 medium green bell pepper, sliced into strips
- 1 medium red bell pepper, sliced into strips
- 1 cup chopped onion, divided
- 3 cloves garlic, minced
- 1 Tbsp. fresh thyme, chopped medium (1 tsp. dried may be substituted)
- 1 Tbsp. fresh oregano, chopped medium (1 tsp. dried may be substituted)
- 1 cup quinoa
- 2 cups reduced-sodium vegetable broth
- Salt and freshly ground black pepper

In skillet, heat 2 teaspoons olive oil over medium-high heat. Add cauliflower, broccoli, peppers, 1/2 cup onion and garlic. Sauté 5 minutes until vegetables start to soften. Stir in herbs and sauté 2 minutes. Remove from stovetop and set aside.

In strainer, place quinoa and rinse thoroughly with cold water. Using your hand, swish quinoa under running water for 2 minutes to remove bitter natural coating. Drain and set aside.

In medium saucepan, heat remaining teaspoon oil over medium-high heat. Add remaining onion. Sauté about 3 to 4 minutes. Add broth and quinoa. Increase heat to bring mixture to boil. Reduce heat to medium-low, cover, and simmer until quinoa is tender, about 20 minutes. Gently stir in vegetable mixture and combine well with quinoa. Season with salt and pepper to taste. Serve.

**Makes 8 Servings**

**Per serving:** 120 calories, 3.5 g total fat (0 g saturated fat), 20 g carbohydrate, 5 g protein, 4 g dietary fiber, 50 mg sodium.

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Likewise, testing a tumor for acquired mutations to help choose the best treatment can also result in uncertain results. Often, there is no drug that is known to match the mutation found, or there may be a drug but it is not available for a particular patient. These uncertainties reflect the fact that genetic testing of both blood and tumor tissue is a very new and promising development in medicine, and it will take time to clarify all of these issues.

If all of this seems a bit confusing, you are not alone. We strongly encourage anyone who is thinking about genetic testing to meet with a certified genetic counselor and healthcare team that is familiar with this type of testing. These specially trained healthcare providers can help you understand all of your options along with the pros and cons linked with any genetic test.

Please call the Risk Assessment Program at 877-627-9684 if you have any questions about genetic testing.
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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MARK YOUR CALENDAR

MAY 14, 2017
Susan G Komen Philadelphia Race for the Cure
https://runsignup.com/Race/PA/Philadelphia/Komen5K

MAY 14 - 20, 2017
National Women’s Health Week
https://www.womenshealth.gov/

JUNE 4, 2017
National Cancer Survivors Day
www.ncsd.org/