

Scott Redding: Welcome to the 3Ps of Cancer podcast, where we'll discuss prevention, preparedness, and progress in cancer treatments and research. Brought to you by the University of Michigan Rogel Cancer Center. I'm Scott Redding. We're here with Dr. Elena Stoffel to talk about genetics and its role in cancer. Dr. Stoffel is an assistant professor of internal medicine in the division of gastroenterology, and is the Director of the Rogel Cancer Center's Cancer Genetics Clinic. Welcome, Elena.

Elena Stoffel: Thanks very much for having me.

Scott Redding: We know that treatments are now targeting genes, but does genetics play a bigger role in cancer outside of that?

Elena Stoffel: It's interesting, when you talk about cancer, cancer is by definition a genetic disease, in that many cancers are caused by alterations that occur in individual cells. So it's such that, when the programming of these cells is thrown off, these cells then grow faster than the cells around them, and start acquiring properties that they shouldn't have, that allow them to move beyond their boundaries and invade. That's what the definition of cancer is, is it is a cancer is a group of cells that are not behaving according to their plan, and are invading beyond the boundaries that they're supposed to be contained by. There are some cancers however ... I should say most cancers acquire these alterations in genes during the course of a person's life.

But, there's a small subset of cancers that arise because a person has inherited one copy of a particular gene that does not work properly. Our knowledge of these cancer genes is expanding. As we do more testing of patients with cancer, we are identifying that approximately 1 in 10 patients who are diagnosed with advanced cancers may have developed their cancers as a result of one of these inherited genetic factors. Our job is to try to identify who those patients are, because if we know this in advance we might be able to intervene early to prevent those cancers from developing.

Scott Redding: If one of my parents had an advanced cancer, be it prostate, breast, colorectal, there's a potential chance that I could get one of those cancers?

Elena Stoffel: When we look at risk factors for cancer, one of the major risk factors we look at is family ... In addition to behavioral factors, and we all know smoking is probably one of the biggest factors implicated in cancer. But, we also look at an individual's family history of cancer. So if, for instance say colon cancer, if you have a parent with colon cancer, statistically your risk for colon cancer is two times higher than the average person. But, there are some families where you see colon cancers marching through the generations, and that people are diagnosed at fairly young ages. In some of those families, we are actually able to identify the specific genetic factor that's being passed down from generation to generation, that's associated with a very high risk for cancer. To answer your question, yes, family history plays an important role in assessing your risk for

cancer, and one of the things that we do is we identify whether that family history looks suspicious for one of these inheritable genetic causes for cancer.

Scott Redding: It sounds like at least, you mentioned colorectal cancer, but are there other certain types of cancers that maybe heredity plays a larger role in potential getting cancer?

Elena Stoffel: Yes. We are learning that there are certain types of cancer in which the genetics does play a larger role. For instance, we know that breast cancer is a very common cancer, and that most women who are diagnosed with breast cancer develop breast cancer just by chance. However, we also know that there are families in which many people develop breast cancer at statistically younger ages, and some families in which there is breast cancer, ovarian cancer, and in particular, male breast cancers, really raise suspicion for an inherited cause. Inherited alterations in the BRCA1 and BRCA2 genes are associated with a very, very high risk for developing breast and ovarian cancer. Certainly, we know that population studies suggest that approximately 1 in every 300 people carries an alteration in one of these genes. So hereditary breast ovarian cancer is one of the most common inherited genetic conditions. Lynch syndrome, otherwise known as hereditary nonpolyposis colorectal cancer, is another very common hereditary syndrome. Again, about 1 in every 300 people walking down the street has these alterations that are associated with an increased risk, not only for colorectal cancer, but also for other cancers, including endometrial cancer, ovarian cancer, as well as other cancer types.

Scott Redding: If I have a family history do I need to ... In my case, if there's a family history of say BRCA, or breast cancer, or prostate cancer in my family, do I need to start getting PSA test earlier than 50, or get colonoscopy earlier than 50 if there's colorectal cancer? When should someone start thinking about with this family history, start getting preventive measures?

Elena Stoffel: That's an excellent question. What I tell patients is, start by talking to your doctor about your family history of cancer, because we know that cancers are common, and about one in every three people will develop cancer at some point in their lifetime. In many cases, even when there are many cancers diagnosed in family members, the pattern of those cancers is not highly suspicious for an inherited factor. But, as I mentioned previously, there are some families in which that pattern of cancer does raise a red flag and say, "Additional genetic evaluation is probably reasonable to do." When we talk about cancer screenings, there are published guidelines about what we should be doing for the average risk individual. There are people whose cancer risk is above average, and one of our best ways to be able to identify that is through family history.

Typically, when we see a patient who has questions about their family history of cancer, our first job is to figure out whether they are at average risk, moderate cancer risk, or high cancer risk. A lot of the inherited genetic conditions that we're

talking about would put people at a very high cancer risk, where we would change screening recommendations, we would start screening at younger ages, we would start doing tests maybe that we wouldn't do for the average person. You asked a question about prostate cancer screening, and prostate cancer screening has been very controversial because of information that various different guidelines have put out regarding the value of prostate cancer screening. If you have a family history of prostate cancer, you would be a candidate for prostate cancer screening.

I think that if you have a family history of prostate cancer and multiple other young offset cancers, say for instance breast cancer, ovarian cancer, prostate cancer, and pancreatic cancer, that might raise suspicion for a possible inherited factor, that we would recommend genetic testing for. So I think in answer to your question, the first place to start is by talking to your doctor about your family history, and asking the question, "Could there be something more going on here than just bad luck?"

Scott Redding: Outside of talking to the doctor, if there is thoughts about maybe, "Boy, I'm noticing a pattern. My grandpa had colorectal cancer, my mom had colorectal cancer, daughter of that grandpa." Should I also be talking to my family about these things, and when's a good time to talk to them?

Elena Stoffel: That is a great point, and I think that we think it is so important for families to actually talk about health history, and for families to talk about the cancer diagnoses in the family. A few years back, the US Surgeon General recommended that Thanksgiving be considered family history day, because that's a good time when the family are all together and everybody can talk about how Aunt Sue is doing. I think that for some people, they might feel a little uncomfortable talking about it at the Thanksgiving dinner table, but I think in general, talking about the family health history is very important. So if Thanksgiving is not a good time, then perhaps you can identify another good time. But, this information can be very helpful in caring for each individual's health.

Scott Redding: So now I've talked to my family at the holidays, I've kind of talked to my doctor I might be a little bit worried. What is this you hear about people ... I know people that have a family history of BRCA and they're 16, 17, 18 getting tested. What exactly is genetic testing and genetic counseling?

Elena Stoffel: For families in which the family history of cancer raises suspicion for a possible inherited factor, we recommend that those families be referred to meet with a genetic specialist. A genetic specialist can be a physician or a genetic counselor with specific knowledge of the diagnosis and management of these inherited cancer syndromes. In the setting of families where there is more breast cancer than one would expect to see by chance, or where you see clusterings of breast and ovarian cancer, we would recommend clinical genetic testing. Usually, the best person to start testing with is a person with a cancer diagnosis, because if

you're able to identify an inherited alteration in a gene, then we have a clear positive test, and we can then test other people in the family to see whether they inherited that same alteration.

As an example, for a family with multiple individuals diagnosed with breast cancer and ovarian cancer, if there is a patient with breast cancer or ovarian cancer who is interested in undergoing genetic testing, that patient would meet with a genetic counselor, would have a blood test drawn that would look for alterations in the BRCA1, BRCA2 genes, as well as possibly other genes that have been implicated in breast and ovarian cancer. If the test comes back showing that there is a pathogenic alteration in, say the BRCA2 gene, then every individual in that patient's family could benefit from genetic testing. The key is to share this information with family members, because it has implications for their management, because people who carry an inherited alteration in, say BRCA1 or BRCA2, would be eligible to start breast cancer screening at around age 25. People would have breast MRIs in addition to mammograms. And, we would think about ovarian cancer risk reduction, which is typically surgical removal of the ovaries after a woman is done with child-bearing.

Scott Redding: My mom had breast cancer. If my sister had breast cancer as well, then it would be wise for my mom maybe to get some testing done to see if maybe I need to get it as well?

Elena Stoffel: Correct. Your mom or your sister, if they both had diagnoses of breast cancer, either one of them could undergo genetic testing. If the testing came back showing no alterations then that's good news, because it means most likely that one of these strongly penetrant genetic conditions is not playing a role. But, if your mom or your sister was found to have an alteration, then we would recommend testing for you, because even men can have their care changed on the basis of a genetic test result. For men with BRCA1 or BRCA2 alterations, the risk for prostate cancer seems to be high enough that we would recommend prostate cancer screening starting at younger ages, typically by age 40.

Scott Redding: So if someone has the BRCA1 or 2 gene mutation, is that something that will guarantee that down the road that they will get breast or ovarian cancer?

Elena Stoffel: No, and I think that it's important to realize that just because a patient has been diagnosed with one inherited altered copy of one of these genes, it does not guarantee that they will develop cancer during the course of their lifetime. Each of us inherits two copies of every gene, we get one from our mother and one from our father. Typically, with two functioning copies of a gene, you have a backup. But, if one copy is not working properly, then you're reliant on that last copy, and if that stops working, that's when the chances of cancer increase. Just because you have one non-working copy does not guarantee that you will get cancer, but it does statistically increase your cancer risk. For that reason, if you have one altered copy, we do follow you much more carefully than we would the average person.

Scott Redding: Say someone has breast cancer and they actually do have that gene, but their initial diagnosis is only in one breast, is there the possibility of it spreading to the second, is that a major concern? What would someone do in those kinds of situations?

Elena Stoffel: That's an excellent question. There were actually some recent studies published that demonstrated that women with BRCA mutations who have been diagnosed with breast cancer have outcomes that are very similar to women who don't have BRCA alterations. I think one of the things to recognize is that if you do have a breast cancer diagnosis, your chances of having a second breast cancer are statistically higher than the average person. If you do have an inherited copy in the BRCA gene, that means that every cell of your body is down to its one backup copy.

So to answer your question, it does not guarantee that you will get a second breast cancer, but your risk for a second breast cancer is higher. And certainly, many women who are diagnosed with BRCA alterations do have very in depth conversations about the risk for a secondary breast cancer, and whether or not surgery to remove the contralateral breast is something that's right for them. This is all very, very personal decision making, and certainly I would encourage women to talk with their doctors about things that they can do to reduce their risk for breast cancer, because while surgery is one of them, there are also medications that can play a role in reducing risk for women for whom surgery is not a great option.

Scott Redding: If I don't live necessarily in the Ann Arbor area, maybe I live up in the UP, and I have concerns about this, how would I find out about where I could maybe get some genetic testing done?

Elena Stoffel: That's a great question. I think that our team here at the University of Michigan has a lot of experience in diagnosis and management of families with a variety of hereditary cancer syndromes. We also work very closely with the Michigan Department of Health and Human Services. Michigan is one of the five states identified by the Centers for Disease Control as a cancer genomics best practices site. So the Michigan Department of Health and Human Services, in conjunction with the Michigan Cancer Genetics Alliance, actually has a website listing providers who deliver cancer genetic services all across the region, and certainly that's a great resource if you have questions about whom near you could be able to help you determine whether or not a cancer genetic evaluation is necessary for you and your family.

Scott Redding: What's that website that they could go to?

Elena Stoffel: The Michigan Genetics Resource Center can be accessed through MIGRC.org.

Scott Redding: So this is a lot of information to take in. What is some kind of key major takeaways we should end with?

Elena Stoffel: I think the key takeaways are the following: number one, cancer is common and most cancers are not associated with inherited genetic factors. However, there are some cancers that are. Identifying who in your family has had cancer diagnoses can help your doctors figure out if there is an increased risk for cancer due to genetic factors in your family. So talk to your family and talk to your doctors about your family history of cancer.

Scott Redding: Great. Well, I really appreciate you taking the time, Elena, today to talk with us, and thank you for the great information.

Elena Stoffel: My pleasure. Thanks so much.

Scott Redding: Thank you for listening and tell us what you think of this podcast by rating and reviewing us. If you have suggestions for additional topics, you can send them to cancercenter@med.umich.edu, or message us on Twitter @UMRogelCancer. You can continue to explore the 3Ps of Cancer by visiting RogelCancerCenter.org.