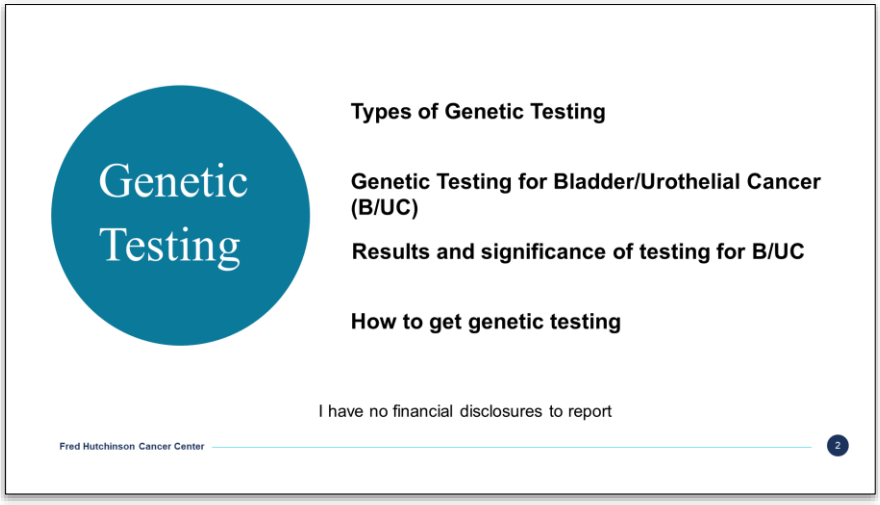
Stephanie Chisolm:

Great. So, Dr. Dubard-Gault, tell us a little bit about what patients should know about genetics and when and how they should connect with a physician who specializes in this. And should they engage genetic counseling?

Dr. Dubard-Gault:

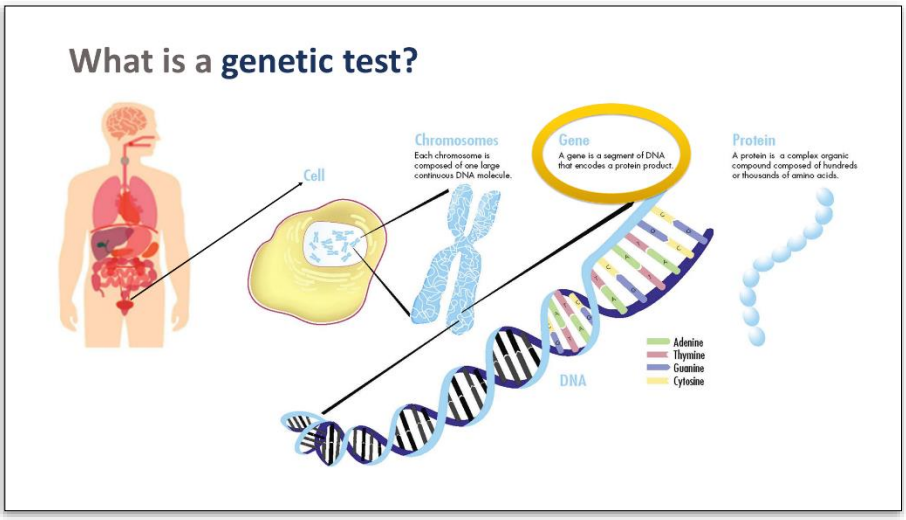
I'll just briefly, because a lot of things have been highlighted already... And thank you Melanie, for sharing your story a little bit in details for what's happened afterwards. I really appreciate that. I trained briefly in medical oncology and genetics, so I have a little bit more of a background to ask questions when there are not enough of an environmental exposure or something that makes it still raise that flag that Dr. Faltas had mentioned, right? So, to really bring all the pieces to the puzzle to explain maybe or find part of the explanation.



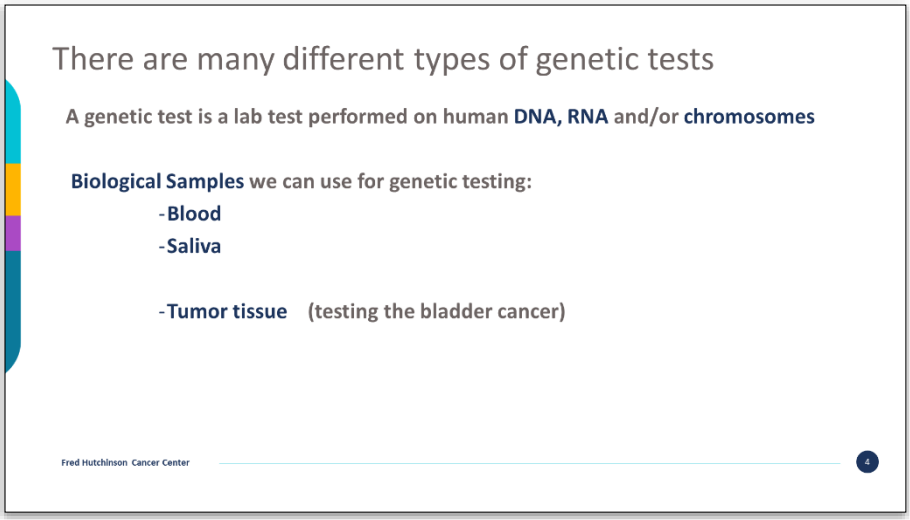
If you could go to the next slide. So, we'll talk briefly about the types of genetic testing. I know Dr. Sonpavde has mentioned a lot of them already. The genetic testing for bladder and urothelial cancer specifically, and the results of what might come your way with that, and then how to get it, how it's done, and all the things that we think about around genetic testing. So, if you could go to the next slide.

Dr. Dubard-Gault:

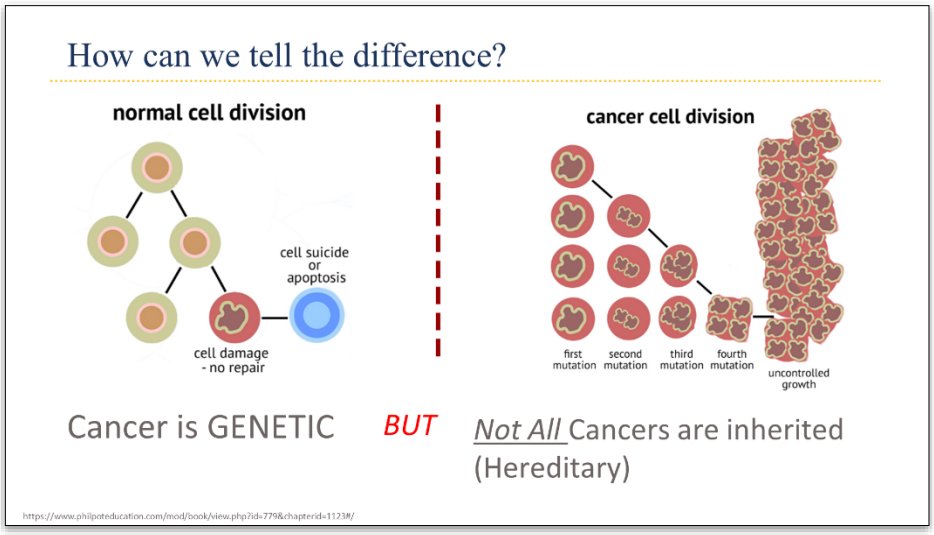
So, I always like to go back to the basics. When it comes to what people are doing at what time and using what sample, it's useful to remember what we're all looking at and what we're looking for. So, the cells that Dr. Sonpavde mentioned originally was really the cells that are from the bladder. And then you isolate the DNA from that, and then the DNA gets transferred onto a testing platform, and then the results come back after all of these things are sequenced to have the results going forward.



So, if you could go to the next slide. And then there are different types of genetic testing. As Dr. Sonpavde mentioned, you could test the tumor, and that is done for people who have a diagnosis of bladder cancer or other cancers. And you can test for DNA. You can also test for another part of the information that we have is RNA or the chromosomes, as I showed you before. And then you can test also for people who have a diagnosis of cancer and/or are unaffected by cancer, like Ken's niece, for example. You could test their blood, you could test their saliva, you could test their nails, and many other samples to test for a predisposition to cancer that is in their genetic makeup that we would not know that they have unless we start looking for them, as Dr. Faltas had mentioned. So, there are many different types.

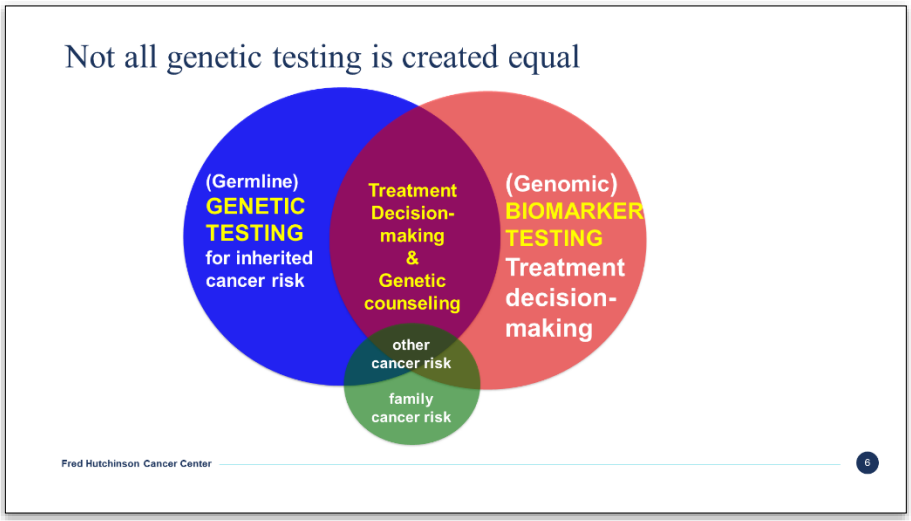


Dr. Dubard-Gault:



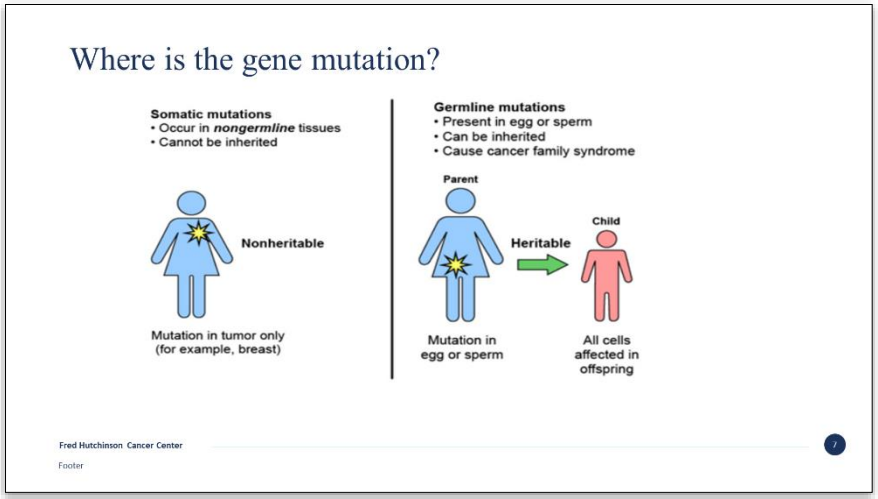
There are many different ways you can go about it. And obviously, each answers you're looking for is based on what samples you're going to look for. So, as we've talked about it, and I agree with Melanie a hundred percent, everything's genetic, right? We are born with a certain amount of genetic mutations and these mutations can very well cause certain things to happen in the right environment or in the wrong environment. And then some of the cells have those protection mechanisms to get rid of any damage or repair the damage before the cells go on. Sometimes though, when that does not happen, you could have a cancer develop, if you go to the next slide, and those mutations will accumulate and cause of cancer. So, in my mind, cancer is genetic for sure, but not all cancers have this inherited component to them that drove the cancer in one direction.

And so there is a distinction between the hereditary kinds of cancer and the cancers that happen by multiple reasons, if you go to the next slide, which is why, and go a little bit further, which is why not all genetic testing is created equal. If you see what's done most often is in the kind of salmon orange color where we want to test the tumor to identify biomarkers or things that will help decide which treatment would work better. If you look on the blue side, sometimes that could be matched with a blood or saliva sample at the same time to look for something inherited that either explains the cancer that is there or partly explains it, or maybe gives a risk to another cancer in the future. And if you go to one more, and sometimes there is something in the middle here that works together to say, okay, from this point on, how do we make sense of this information and how do we go forward with genetic counseling? As Ken mentioned, and Melanie, how do we make sense of this information, and how do we turn it into an action plan?

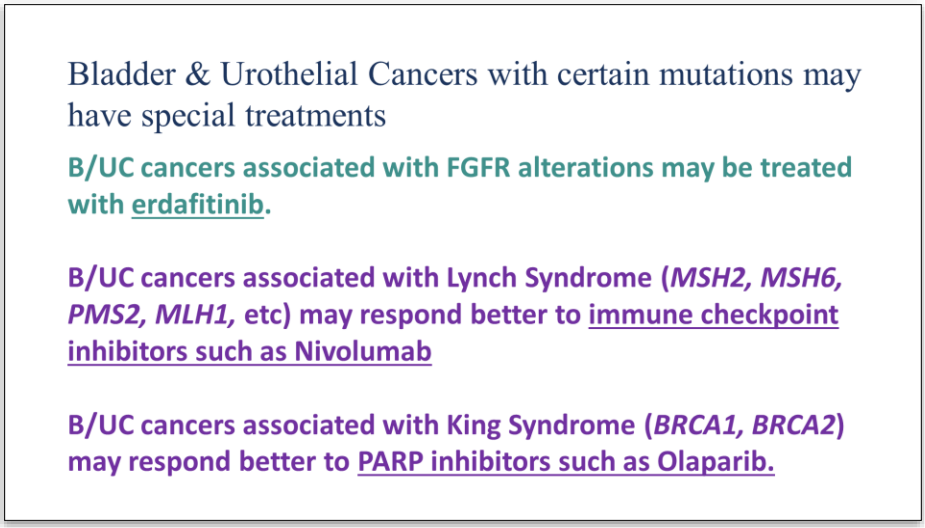


Dr. Dubard-Gault:

Yeah, exactly. Go to the next slide. Now, I think the important part here is also, as this has been mentioned already, is where is the genetic mutation? Is it solely or only in the tumor, the bladder cancer or the breast cancer or the pancreatic cancer, or is it part of the makeup that is passed down from one generation to the next? We know in the cancer genes that we are all talking about, these tend to be passed down from one generation to the next. So, it's most often, as Melanie shared, that it was inherited from the generation prior, either biological paternal side or biological maternal side, and it really helps then also test other family members to make sure that they can take actions as well for their own either screening or treatment if they were to need it.

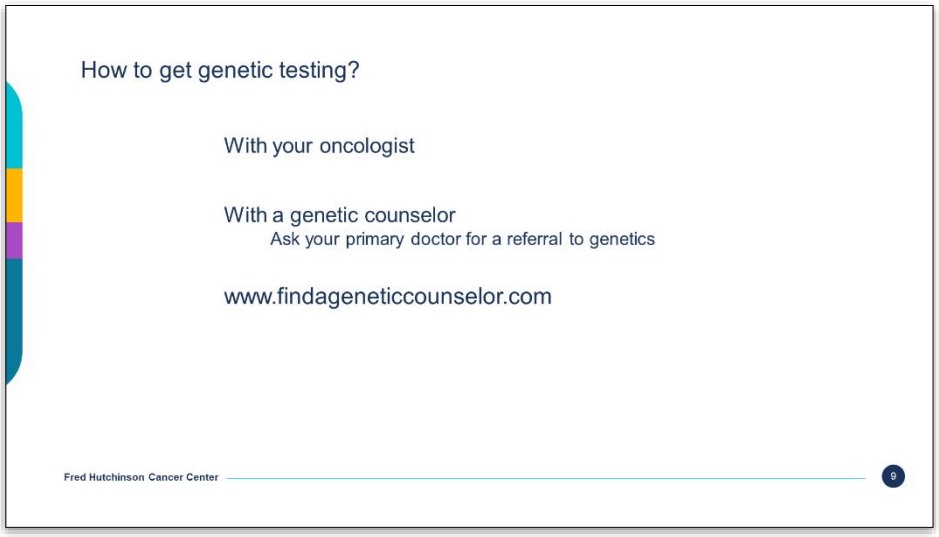


And then I won't go into too many details about this because Dr. Sonpavde did mentioned, but really knowing this information is really useful for picking the right medication, whether it is an immune checkpoint, as Melanie mentioned, or PARP inhibitor as in the Atlantis trial, or other medications that are coming on and being available for treatments of bladder cancer.



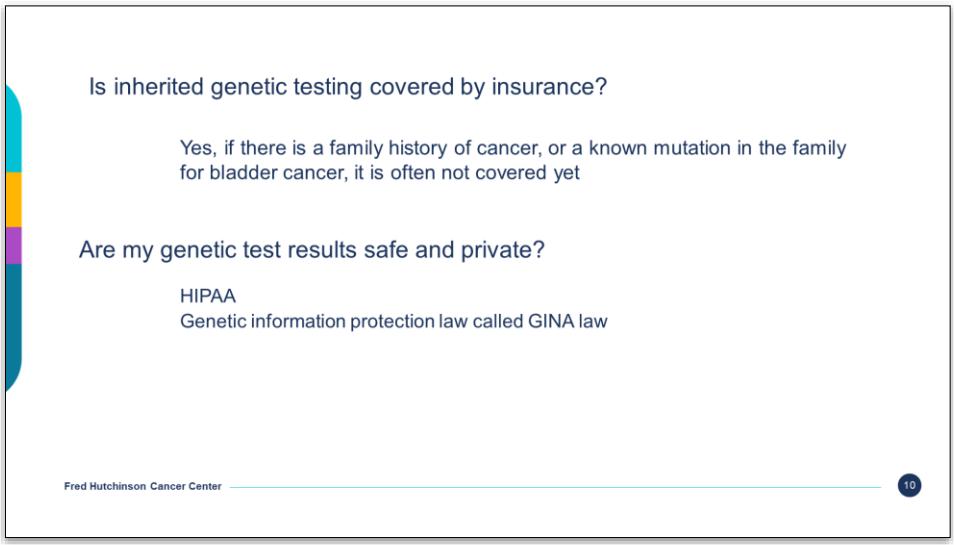
Dr. Dubard-Gault:

So, how do we get genetic testing? Number one would be with your oncologist who feels comfortable, has experience in ordering genetic testing. Number two would be to be referred either by your oncologist or your primary doctor or self, by your yourself to a genetic counselor. And genetic counselors are exactly the right person to help review your family history and decide how likely it is that you will have a positive genetic result and what that positive genetic result would mean and help you through the process of getting that testing done, whether it is on the tumor, on the blood or saliva, or as a combination of the two, to really get to the implications of the results and what they mean for the treatment and the family members.



And then I think this is a resource that is underutilized, but findageneticcounselor.com is a website that was established by the National Society of Genetic Counselors to really help people out there find a genetic counselor near them, whether it is on telemedicine or in person. Every single state has genetic counselors, and so that's an easy way to find them. If you go to the next slide.

And then the two things that I want to mention there briefly, because this comes up every single time, is genetic testing covered by my insurance. And in the cases where you have a family history, most often, the genetic testing will be covered. Or if there's a known mutation as Dr. Sonpavde mentioned, or as in Ken's story, then for sure the genetic testing will be covered, but it is often that for bladder cancer, the genetic testing is not covered yet, meaning that sometimes, you'll have to have an out of pocket cost or pay for the testing yourself, especially if some of these criteria are not met, until we get to the time where we will test everyone every time when they're diagnosed with a cancer.

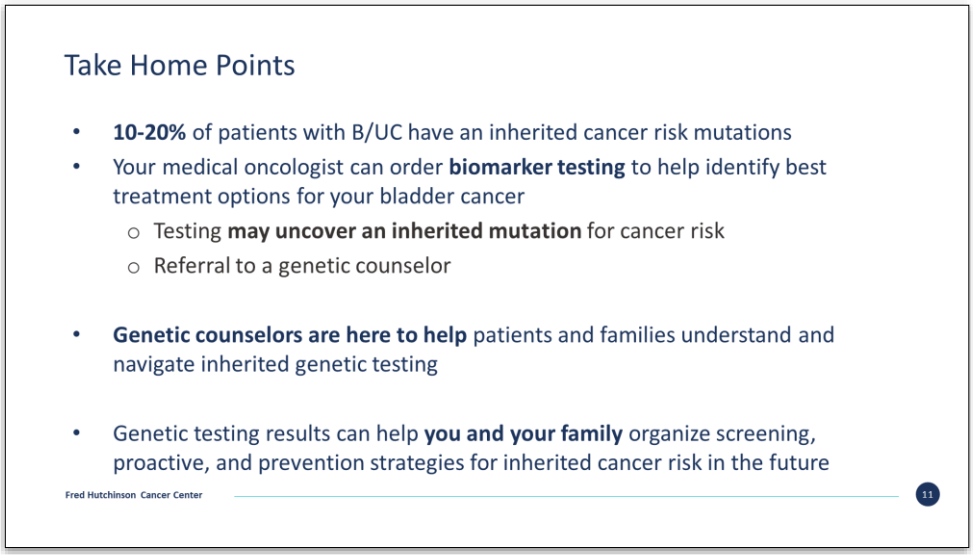


And the other thing I'll mention there is that sometimes the genetics clinic will not be able to see patients with bladder or cancer because of the busyness of the clinic, and sometimes this is something that can be done separately through a website or another mechanism to be able to get the genetic

testing part of things. And then where are the genetic testing results stored? Are they safe? And who has access to them?

Dr. Dubard-Gault:

So, the genetic results are clinical medical tests, and so they are safely saved in your chart. They're only shared with who you'd like them to be shared with, and they're private. So, they're protected under the HIPAA, protection law for confidentiality, and also under the GINA law that is for protecting genetic information specifically. So, this information is not utilized for healthcare coverage or for employment if the person is still working or family members are looking for a job.



And I think that is my last slide. And so the take home points to really bring all of these thoughts that we've put together is that between 10 and 20 patients with bladder and urothelial cancer have an inherited cancer gene mutation. Your medical oncologist can order your biomarker testing to help identify the best treatment. Sometimes that will uncover an inherited mutation and will refer you to a genetic counselor to discuss how to confirm that and to take the next appropriate steps. Genetic counselors are amazing. Thank you, Melanie. They're here to help you and your family understand the meaning of the results and to take the next steps for early screening and detection. And obviously, the genetic testing results can help you and your family for the future. And I'll stop there. Thank you.

Stephanie Chisolm:

Wow, this has been an incredibly comprehensive discussion. I really do appreciate it.