PHYSICIAN SPECIALISTS NORTHWEST

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HEREDITARY CANCER GENETIC TESTING

About 5-10% of all cancers have an inherited genetic basis that can in turn be passed on to offspring and shared with other blood relatives. Genetic testing involves obtaining either a saliva or blood test to evaluate the DNA for possible mutations (variants) that, if present, can be associated with increased cancer risks of different types. Cancer risks are specific to each specific mutation and, depending on the panel that is ordered, may indicate increased risk for breast, uterine, ovarian, colon, pancreatic, endocrine, genitourinary, skin, brain/nervous system, sarcoma or hematologic cancers among other cancer risks. The goal of testing is to determine whether you have a currently identifiable gene mutation. A negative result does not necessarily eliminate your risk of cancer. It is very important and helpful for you to do a careful review of your family history prior to your appointment, noting mostly cancer types and age of diagnosis in the family.

Genetic testing generally involves testing for several different genes with one test. We call this list of genes a panel. There are different labs that do the testing and the panels they offer are not the same. Also, there are some differences in their billing policies. All the labs are CLIA certified and CAP accredited, and we refer to different labs in consideration of your specific situation. In general, we prefer to test the person in the family that has had cancer if possible. If that person is not available, the next best person to test would be a first degree relative, and if that person declines or is not available, a second degree relative can be tested.

Some of the labs offer an option for a narrower panel with a more limited number of genes on the panel (looking for mutations that are associated with more common cancers), versus a broader panel, looking for gene mutations that are associated with less common or rare cancers. When a larger panel is selected, there is more of a chance that guidelines for management may be less clear. Also, there is more of a chance that we might identify variants of unknown/uncertain significance (which will be discussed later, and which are not actionable). Depending on your knowledge of your family history as well as patterns of cancer in your family, and your personal preference, there may be more of a consideration to do one panel over another.

Most insurers will cover genetic testing with little out of pocket if you meet established guidelines for genetic testing. The lab confirms insurance coverage and notifies you of your anticipated out-of-pocket cost at the time your orders are placed. If this cost is too high, you have an option to revert to a cash option in most cases for around $250. There is also generally a financial assistance option which our staff can help you understand. You are solely responsible for knowing and agreeing to costs billed by the lab as the lab is not connected with Dr. Smith's practice. The results take approximately 10-21 days for a routine test (but can take longer depending on your insurance), and about 7-10 days for a STAT test. Dr. Smith will text you when the results are in to discuss.

There can be technical limitations to the testing, and it is possible that there may be mutations that are

not yet discovered which could be identified later. So, it is a consideration in some cases, for you to do update testing at some point in the future if new genes are discovered. We have a consent form which we will ask you to read and review. If you agree to proceed with the test, we will ask you to sign the consent. Your results will be disclosed through a secure portal with the lab (instructions for access to the portal will be given at the time the specimen is collected). The results can be benign (no harmful mutations), pathogenic (harmful mutation), likely pathogenic (90% likelihood harmful mutation), or variant of unknown/uncertain significance (VUS). Most of these gene mutations are autosomal dominant, which means that it only takes one abnormal copy of the gene from either mom or dad to convey risk to you. A few of these mutations are autosomal recessive (labeled biallelic in the gene list). This means that for you to experience risk from these mutations you need to inherit an abnormal gene mutation from both mom and dad.

Unless there is a known mutation in the family, a negative result means that there is no known genetic risk currently, and we call this an **uninformative negative** result. Sometimes, in this setting, we will recommend testing other family members to clarify the possible existence of a pathogenic (harmful) mutation in the family. Family members who desire or need testing can text or call our office if they live in Idaho or Washington state (208-400-5131) or if they live outside of our region, they can find a genetic counselor at this web address: (http://nsgc.org/findageneticcounselor). An uninformative negative result does not completely rule out hereditary risk since there is a possibility that there could be some currently undiscovered mutation. We still manage you clinically based on your personal and family history. A **true negative** result means that there is a known mutation in the family, and you do not carry this known mutation. In other words, there is a mutation that explains the familial cancer history, and you did not inherit this mutation. In this setting, your cancer risk drops to normal population risk.

A **positive result (harmful mutation—pathogenic/likely pathogenic variant)** will often lead to a recommendation for increased surveillance and sometimes for risk reducing medication or in some cases risk reducing surgery. Recommendations are based on national guidelines where available. If you have a positive result (harmful mutation), we will facilitate referral to the lab's designated genetic counselor or a regional certified genetic counselor. After that, Dr. Smith recommends following up to develop and implement your care plan, and subsequently annual follow up. If you have a harmful mutation, the lab provides a genetic counseling consultation that is included in the cost of your testing.

There may also be a finding of **variant of uncertain/unknown significance (VUS)** or multiple variants of uncertain significance. This is a change (or changes) in the DNA that has not yet been classified as either harmful or benign and is detected at least 20% of the time. Many of these prove ultimately to be benign changes later, as more data is collected. However, a small percentage of these may ultimately prove to be harmful, which would then prompt a change in your management and testing of other blood relatives. If your report shows a variant of uncertain significance (or multiple variants of uncertain significance), we do not change your management on that basis, unless this is later reclassified. I recommend that you stay in contact annually with the lab to update them on any change of address and to check whether your VUS has been reclassified. If you have further questions about this VUS, the lab does provide a genetic counseling consultation that is included in the cost of your testing.

The genetic information non-discrimination act (GINA)* is a federal law that was enacted in 2008 that prohibits most health insurance providers from using an individual's genetic information to determine

health insurance eligibility, health insurance premiums, contribution amounts or coverage terms. GINA prohibits most employers from using an individual's genetic information to make decisions about that person's pay or other employment status. GINA does not apply to life insurance, disability insurance, or long-term care insurance.

Please let Dr. Smith know if you have any questions or concerns. You can also reach out directly to the lab. Our goal is to give you the best possible care, and we would like to hear from you if there is something else that you need. If you are expecting a call from us and do not hear within a few days of your expected call, please call us to ensure that proper action is taken on any issue of concern.

*Genetic Information Nondiscrimination Act of 2008 (GINA). Vol. Public Law No.110-233. More information at: https://www.ashg.org/advocacy/gina/

Best Regards,

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DR. F. AMES SMITH JR. MD