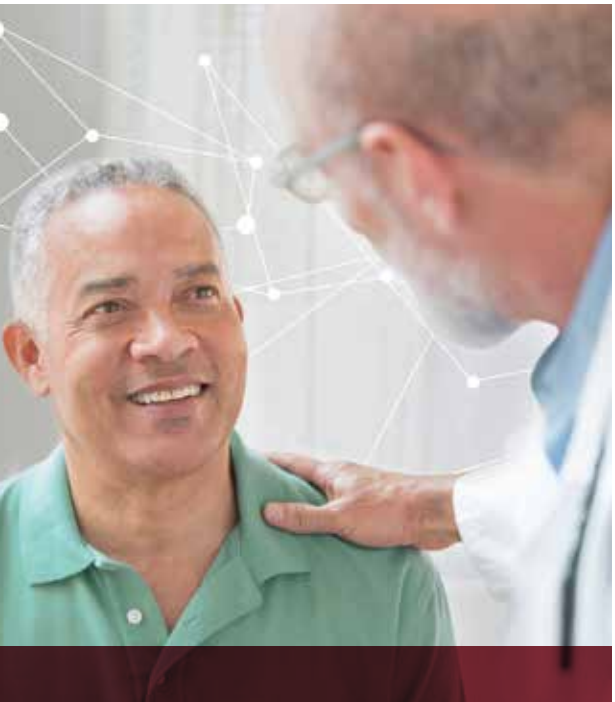


Cancer Testing Solutions

A guide to genetic testing for hereditary cancers

The benefit of knowing

Sonora Quest Laboratories™
A Subsidiary of Laboratory Sciences of Arizona

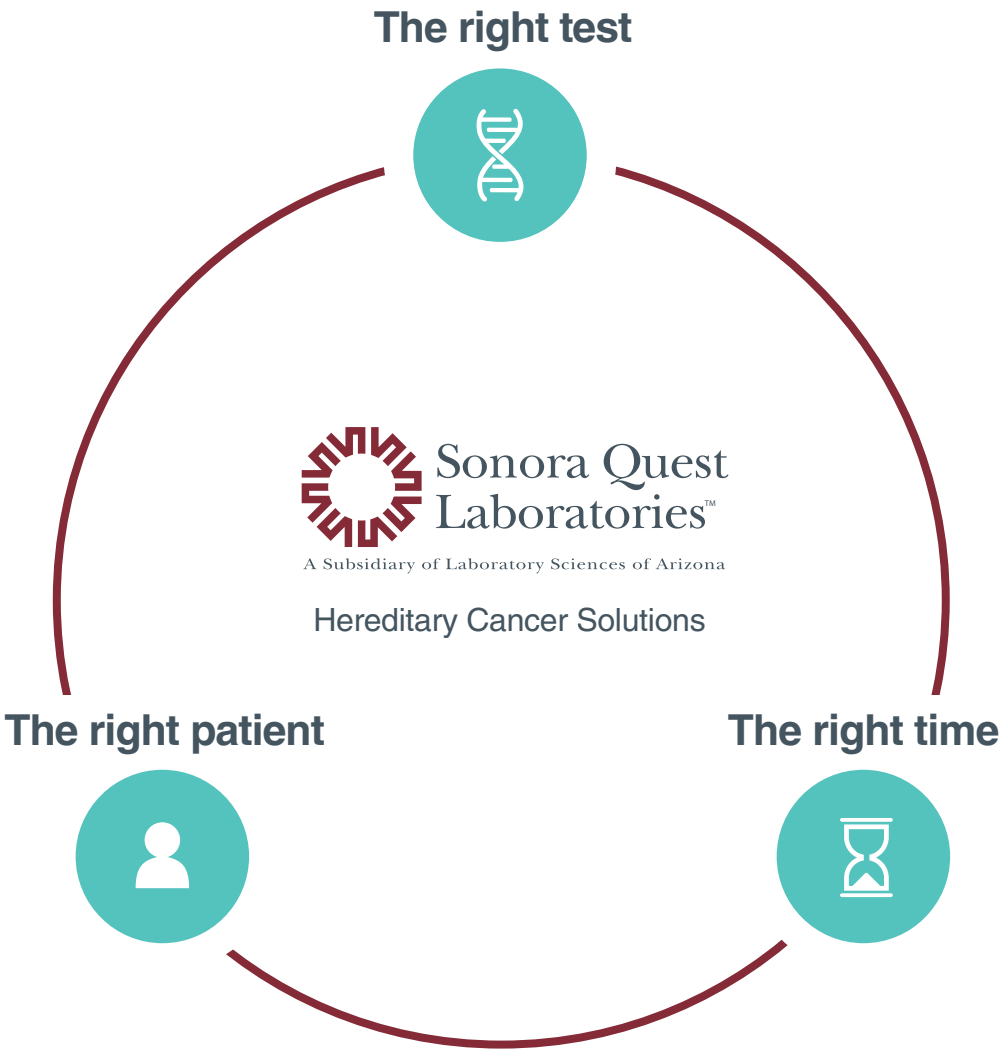
Hereditary cancer genetic testing can play a critical role in managing health

Cancer touches millions of Americans each year. Many people wonder about their own risk of developing cancer. For some patients, genetic testing plays an important role in clarifying that risk. It's important to choose the **right test** for the **right patient** at the **right time.** This guide highlights important points to consider when choosing a genetic test.

Why consider genetic testing

The decision to pursue genetic testing is a personal one. A patient's current medical status, personal experiences with cancer, and general readiness for genetic information all influence this process.

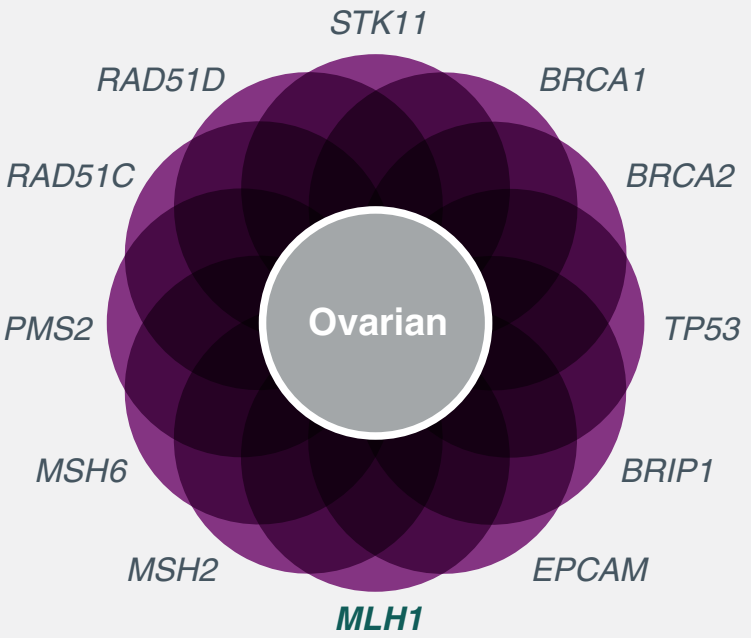
For some patients, genetic testing can provide the information needed to tailor their screening regimen and open the door to risk-reduction options. However, genetic testing also has the potential for less clear-cut results or variants of unknown clinical significance (VUS) which may not inform medical management. Having an open dialogue with your patients about these topics can assist with shared decision-making.



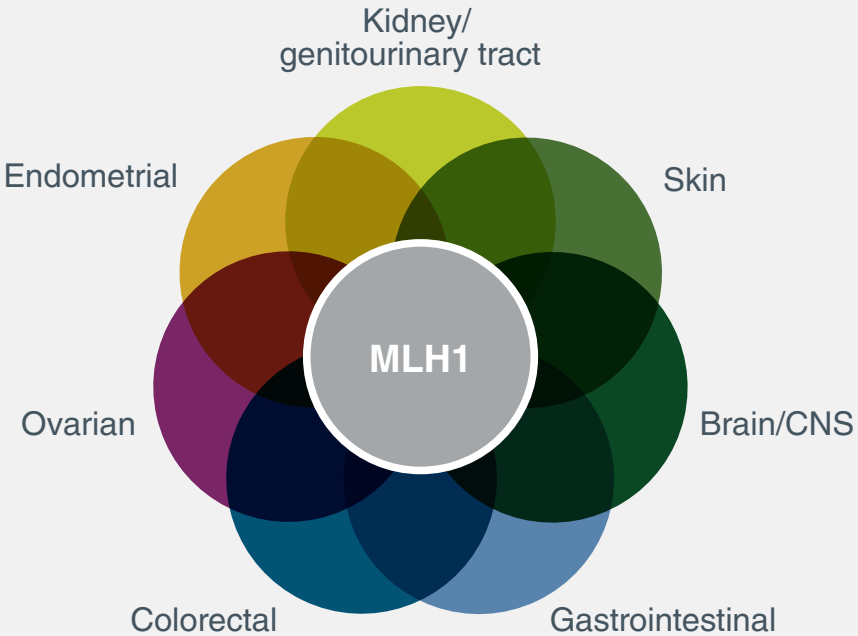
Making sense of genetic testing

One **type** of cancer can be caused by several cancer genes, and one gene can cause several different **types** of cancers. Here is an example highlighting the connection between various hereditary cancers and genes.

Ovarian cancer can be caused by many genes



The *MLH1* gene can cause a variety of cancers



Choosing the right patient

Do any of the following apply to your patient?

Current or past diagnosis of cancer

- ☐ Cancer diagnosed under age 50
- ☐ Bilateral or multiple primary cancers
- ☐ Rare cancer
  (eg, male breast cancer, ovarian cancer, pheochromocytoma)
- ☐ Cancer diagnosed at any age and significant family history
- ☐ Ashkenazi Jewish ancestry

→ **Yes** → Discuss genetic testing: patient possibly high risk

→ **No** → Manage based on family history

Family history of cancer

- ☐ ≥ 3 relatives with a related cancer on the same side of the family
- ☐ ≥ 2 relatives with a related cancer, 1 diagnosed under age 50
- ☐ Relative with a known familial variant
- ☐ Ashkenazi Jewish ancestry

→ **Yes** → Discuss genetic testing: patient possibly high risk

→ **No** → Manage based on family history

Choosing the right test

Discuss benefits and limitations of genetic testing with patient *or* refer for genetic counseling

High-risk personal and/or family history

History consistent with multiple cancer syndromes *or* history not explained by previous genetic testing

Comprehensive and Guideline-Based Hereditary Cancer panels

High-, moderate-, and emerging-risk genes: includes the focused panel and single syndromes, as well as genes that may lack specific risk information and management recommendations. These may be further defined over time.

History includes primarily 1 cancer type

Cancer-specific panels

High- and moderate-risk genes: most have well-established cancer risks and management guidelines are established. Some cancer risks may not be as well-characterized.

History is suspicious for a well-characterized hereditary cancer syndrome

Hereditary cancer syndrome tests

Syndrome-specific tests that analyze genes associated with well-characterized cancer syndromes.

Patient has a relative with a familial mutation

Hereditary cancer single site test

Only looks for variant previously identified in a relative.

Additional considerations/actions:

- Begin genetic testing with an affected individual whenever possible
- Threshold for testing may be lower for certain ethnicities or family situations (adoption, small families)
- Guidelines strongly recommend genetic counseling
- Refer to the **National Comprehensive Cancer Network®** (NCCN) guidelines for more detailed selection criteria
- Revisit genetic testing options regularly

Testing options

Need additional assistance?

Call Quest Genomics Client Services* at **866.GENE.INFO** to speak with a genetic counselor.

66 and 32 genes (respectively) including high-risk, moderate-risk, and emerging genes associated with a broad spectrum of hereditary cancers

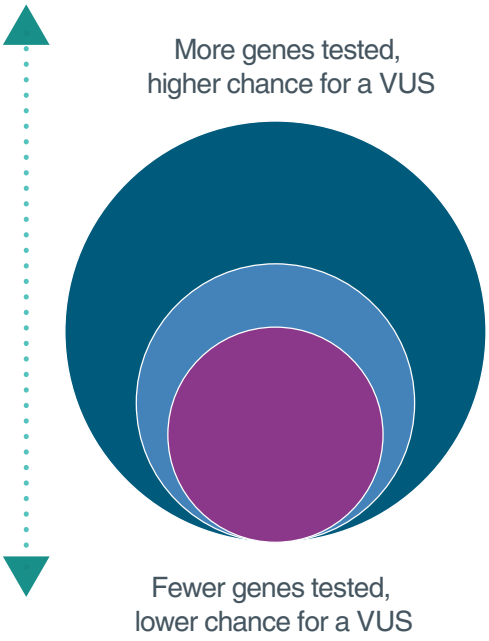
Hereditary Colorectal Cancer Panel: 19 genes
associated with increased risk for colorectal cancer

Syndrome-specific tests that analyze genes associated with well-characterized cancer syndromes such as Lynch Syndrome

Single-site testing is available when there is a known variant in the family.
This test is available for any of the 66 genes on our Comprehensive Hereditary Cancer Panel.

VUS Rate by Test Type

- **Comprehensive and Guideline-Based Hereditary cancer panels**
- **Cancer-specific panels**
- **Hereditary cancer syndrome tests**



*Available through one of our parent companies, Quest Diagnostics.

What the results mean

Types of results		Insights
+	**Pathogenic/ likely pathogenic variant**	• Lifetime cancer risk **elevated** • Increased cancer risk(s) are gene-specific
-	**Negative** No clinically significant variants identified	• Patient previously diagnosed with cancer - Cancer risk based on personal and family history • Patient with a family history of cancer only (no personal history) - When possible, testing an affected family member is recommended for a more informative risk assessment - Cancer risk based on personal and family history
VUS	**Variant(s) of unknown clinical significance (VUS)**	• A genetic change that is not well-characterized. May or may not be associated with increased cancer risk. A VUS may be further defined over time.

What steps to consider

Testing outcomes		Actions
+	**Positive test result for high-/moderate-risk gene**	• Review medical management guidelines - Includes surveillance, chemoprevention, and/or risk-reducing surgery • Refer to specialty oncology center • Genetic counseling and testing for at-risk family members is recommended
+	**Positive test result for emerging-risk gene**	• Medical management based on personal and family history • Revisit literature regularly for developing guidelines
VUS	**Variant(s) of unknown clinical significance**	• Should **not** influence medical management decisions • Medical management based on personal and family history • Reclassified variants will be communicated to the ordering provider. Inquiries about variant status can be made to 1.866.GENE.INFO (1.866.436.3463).
-	**Negative test result**	• Additional genetic testing may be appropriate for patient or affected relative if inherited cancer is strongly suspected • Medical management based on personal and family history
×	**Patient declines testing**	• Discuss medical management options - Tools to assist in this assessment include NCCN®, Gail model, Tyrer-Cusick, Claus tables, CanRisk • Refer to specialty oncology center • Genetic counseling for family members is advised • Revisit genetic testing options regularly • Update personal and family histories regularly

A result is only as good as the action it inspires.

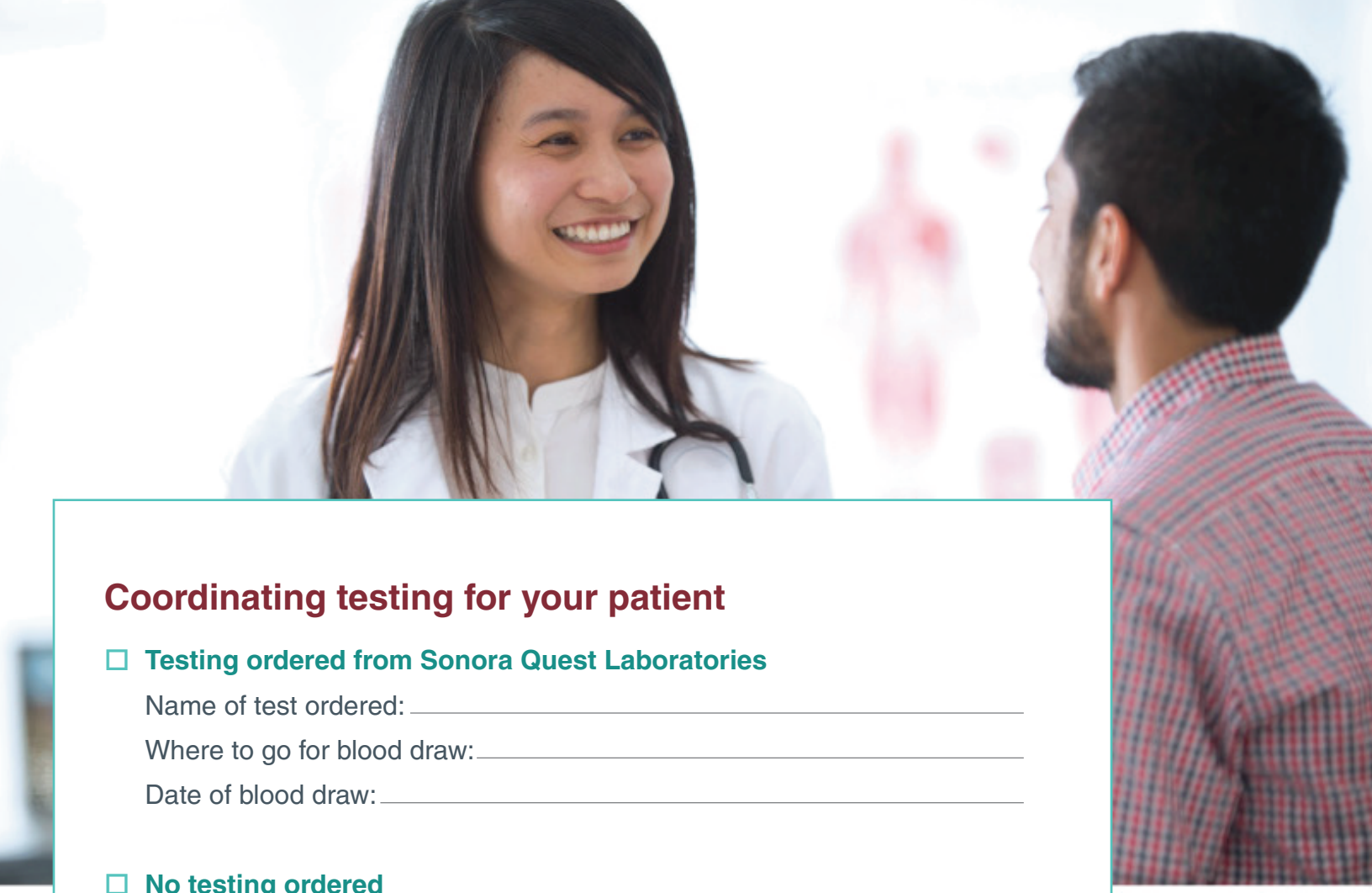
Call Quest Genomics Client Services* at **1.866.GENE.INFO (1.866.436.3463)** to speak with a genetic counselor.

*Available through one of our parent companies, Quest Diagnostics.

Hereditary Cancer Test Menu

Sonora Quest Laboratories offers a large test menu, giving the flexibility to select the right test for your patient at the right time.

Test offering	Test code
Comprehensive and Guideline-Based Hereditary Cancer panels	
Comprehensive Hereditary Cancer Panel (66 genes) *APC, ATM, AXIN2, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN1B, CDKN2A, CHEK2, DICER1, EGFR, EPCAM, FANCA, FANCC, FANCM, FH, FLCN, GALNT12, GREM1, HOXB13, MAX, MEN1, MET, MITF, MLH1, MRE11 (MRE11A), MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NTHL1, PALB2, PMS2, POLD1, POLE, POT1, PTCH1, PTEN, RAD50, RAD51C, RAD51D, RECQL, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, STK11, SUFU, TMEM127, TP53, TSC1, TSC2, VHL, XRCC2*	907263
Guideline-Based Hereditary Cancer Panel (32 genes) *APC, ATM, AXIN2, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A (p16,p14), CHEK2, EPCAM, GREM1, HOXB13, MLH1, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NTHL1, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53*	907261
Cancer-specific panel	
Hereditary Colorectal Cancer Panel (19 genes) *APC, AXIN2, BMPR1A, CDH1, EPCAM, GREM1, MLH1, MSH2, MSH3, MSH6, MUTYH, NTHL1, PMS2, POLD1, POLE, PTEN, SMAD4, STK11, TP53*	907262
Hereditary cancer syndrome tests	
Breast cancer syndrome	
BRCA Panel (BRCA1, BRCA2) *BRCA1, BRCA2*	906369
BRCA Ashkenazi Jewish Screen Common founder variants *BRCA1 c.68_69delAG, BRCA1 c.5266dupC, BRCA2 c.5946delT*	906366
BRCA Ashkenazi Jewish Screen w/Reflex to BRCA Panel (BRCA1, BRCA2) Ashkenazi Jewish screen; if negative reflex to BRCA Panel-*BRCA1* and *BRCA2*	906474
BRCA1 and BRCA2 Deletion and Duplication Detects large deletions/duplications in the *BRCA1* and *BRCA2* genes which are not detectable by DNA sequencing	906367
Lynch syndrome	
Lynch Syndrome Panel (5 genes) *MLH1, MSH2, MSH6, PMS2,* and *EPCAM* (deletion/duplication only)	906541
Other cancer risk	
Hereditary Cancer Single Site(s) *APC, ATM, AXIN2, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN1B, CDKN2A (p16, p14), CHEK2, DICER1, EGFR, EPCAM, FANCA, FANCC, FANCM, FH, FLCN, GALNT12, GREM1, HOXB13, MAX, MEN1, MET, MITF, MLH1, MRE11 (MRE11A), MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NTHL1, PALB2, PMS2, POLD1, POLE, POT1, PTCH1, PTEN, RAD50, RAD51C, RAD51D, RECQL, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, STK11, SUFU, TMEM127, TP53, TSC1, TSC2, VHL, XRCC2*	907051



Coordinating testing for your patient

☐ **Testing ordered from Sonora Quest Laboratories**

Name of test ordered: _____

Where to go for blood draw: _____

Date of blood draw: _____

☐ **No testing ordered**

Update personal and family histories regularly

Revisit genetic testing options regularly

Next appointment is: _____

Call with questions: _____

Helpful information resources

National Comprehensive Cancer Network (NCCN): NCCN.org

National Society of Genetic Counselors (NSGC): NSGC.org

Facing Our Risk of Cancer Empowered (FORCE): Facingourrisk.org

Bright Pink: Brightpink.org

American Cancer Society: Cancer.org

Sonora Quest Laboratories™

A Subsidiary of Laboratory Sciences of Arizona

Sonora Quest Cancer Testing Solutions:

when you need to know more, you'll find more here

The more you know about your patient's risk of hereditary cancer, the more you can do and the better you can navigate the next steps together. As one of Arizona's largest providers of clinical laboratory testing services, our diagnostic insights reveal new avenues to identify and treat disease, inspire healthy behaviors, and improve healthcare management. Our complete portfolio of hereditary cancer tests, services, and expert analysis helps you understand patient risk, and is just the first step in our approach to patient care.

For more information please contact your Sonora Quest Account Manager or visit SonoraQuest.com

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