Quest Advanced® Oncology

A guide to **genetic testing** for hereditary cancers

For a clear understanding of risk

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

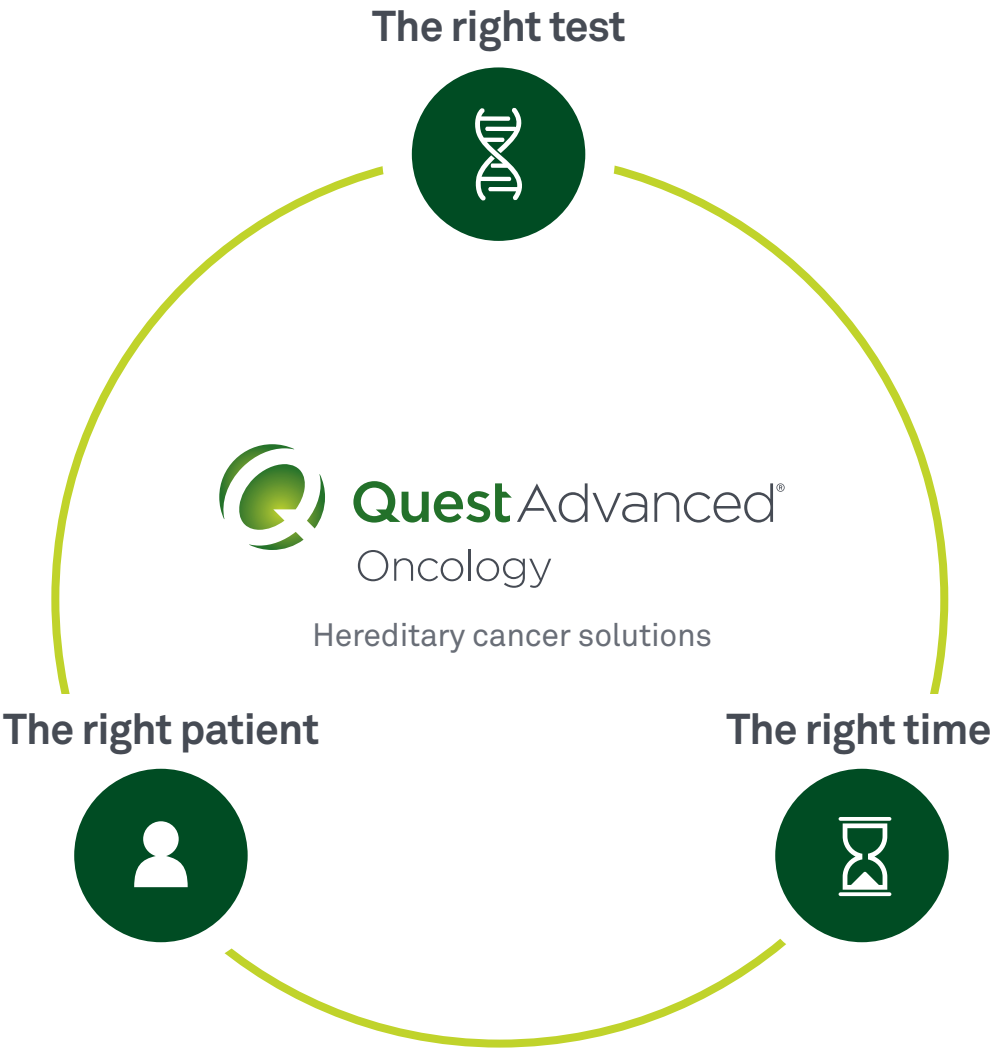
Cancer touches millions of Americans each year. Many people wonder about their own risk of developing cancer. For some patients, genetic testing plays an important role in clarifying that risk. It's important to choose the **right test** for the **right patient** at the **right time**. This guide highlights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

1.866.GENE.INFO (1.866.436.3463)

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.

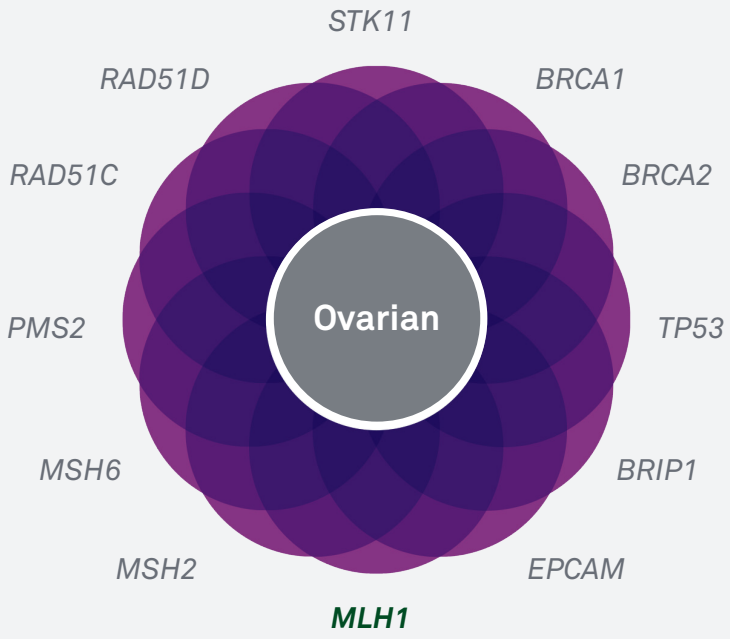
For some patients, genetic testing can provide the information needed to tailor their screening regimen and open the door to risk-reduction options. However, genetic testing also has the potential for less clear-cut results or variants of unknown clinical significance (VUS) which may not inform medical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



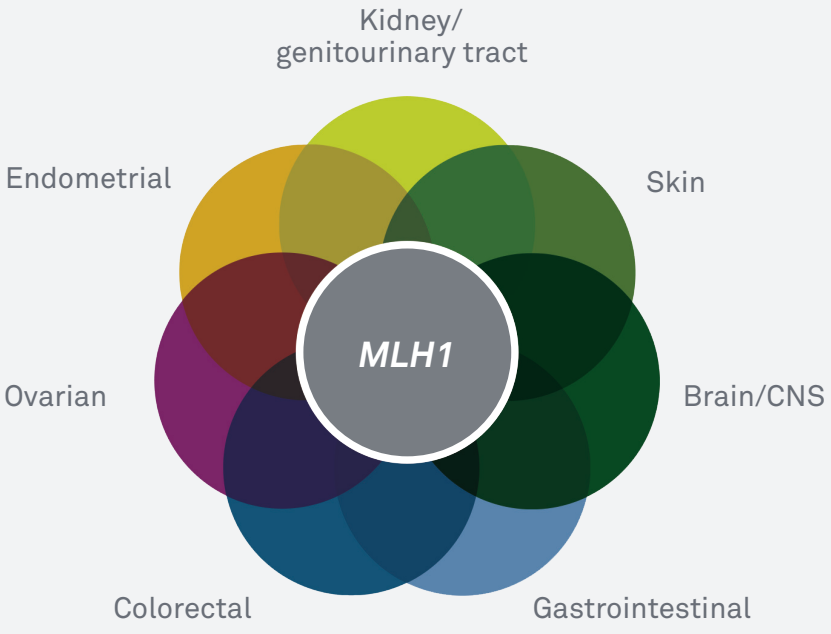
Making sense of genetic testing

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



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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 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

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Testing options

Need additional assistance?

Call Quest Genomics Client Services at **1.866.GENE.INFO (1.866.436.3463)** 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 Breast Cancer Panel: 16 genes associated with increased risk of breast cancer

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

Hereditary Endocrine Cancer Panel: 12 genes associated with increased risk for paragangliomas, pheochromocytomas, and endocrine cancer

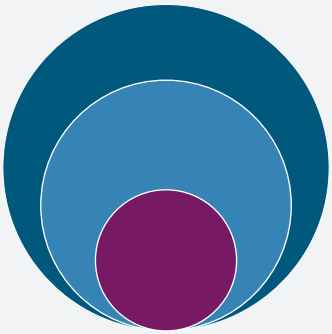
Syndrome-specific tests that analyze genes associated with well-characterized cancer syndromes such as Tuberous Sclerosis Complex (TSC), Lynch syndrome, familial adenomatous polyposis, and others

Refer to **QuestHereditaryCancer.com**

VUS rate by test type

- **Comprehensive and guideline-based hereditary cancer panels**
- **Cancer-specific panels**
- **Hereditary cancer syndrome tests**

More genes tested, higher chance for a VUS



Fewer genes tested, lower chance for a VUS

What the results mean

Types of results		Insights
+	**Pathogenic/ likely pathogenic variant**	• Lifetime cancer risk is **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-Cuzick, 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.

Quest Advanced® Oncology

Hereditary cancer complete genetic testing menu

Quest Diagnostics® offers a large test menu, giving you the flexibility to select the right test for your patient at the right time. For the complete test menu, go to **QuestHereditaryCancer.com**.

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*	38600
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*	38611
Cancer-specific panels	
Hereditary Breast Cancer Panel (16 genes) *ATM, BRCA1, BRCA2, CDH1, CHEK2, EPCAM, MLH1, MSH2, MSH6, NBN, NF1, PALB2, PMS2, PTEN, STK11, TP53*	38621
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*	38631
Hereditary Endocrine Cancer Panel (12 genes) *FH, MAX, MEN1, NF1, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127, VHL*	38641
BRCA Panel Plus (7 genes) *BRCA1, BRCA2, CDH1, PALB2, PTEN, STK11, TP53*	92587

Additional hereditary cancer risk tests	
BRCA Panel (*BRCA1, BRCA2*) *BRCA1, BRCA2*	91863
BRCA Ashkenazi Jewish Screen Common founder variants *BRCA1* c.68_69delAG, *BRCA1* c.5266dupC, *BRCA2* c.5946delT	91864
BRCA Ashkenazi Jewish Screen w/Reflex to BRCA Panel (*BRCA1, BRCA2*) Ashkenazi Jewish screen; if negative reflex to BRCA Panel-*BRCA1* and *BRCA2*	92140
Lynch Syndrome Panel (5 genes) *MLH1, MSH2, MSH6, PMS2,* and *EPCAM* (deletion/duplication only)	91461
Nevoid Basal Cell Carcinoma (NBCCS) (Gorlin) Syndrome Panel (*PTCH1, SUFU*) *PTCH1, SUFU*	38651
Tuberous Sclerosis Complex Panel (*TSC1, TSC2*) *TSC1*, *TSC2*	38661
Juvenile Polyposis Panel (*BMPR1A, SMAD4*) *BMPR1A, SMAD4*	94053
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*	93945
Single-gene tests *APC* – 93797, *ATM* – 38802, *BAP1* – 38803, *BLM* – 38804, *CDH1* – 92568, *CDKN2A* – 93939, *CHEK2* – 93940, *EPCAM/MSH2* – 91471, *FH* – 38805, *FLCN* – 38806, *HOXB13* – 38807, *MEN1* – 93942, *MITF* – 38808, *MLH1* – 91460, *MSH6* – 91458, *MUTYH* – 93944, *NF1* – 93941, *PALB2* – 92571, *PMS2* – 91457, *PTEN* – 92566, *RET* – 93796, *SMARCA4* – 38809, *STK11* – 92565, *TP53* – 92560, *VHL* – 93943	

Coordinating testing for your patient

❑ **Testing ordered from Quest Diagnostics**

Name of test ordered: _____

Date of blood draw: _____

Where to go for blood draw: _____

❑ **No testing ordered**

Update personal and family histories regularly

Revisit genetic testing options regularly

Next appointment is: _____

Call with questions:

_____

QuestHereditaryCancer.com

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Helpful resources

- National Comprehensive Cancer Network (NCCN): NCCN.org
- National Society of Genetic Counselors (NSGC): NSGC.org
- Quest Diagnostics: QuestHereditaryCancer.com
- Facing Our Risk of Cancer Empowered (FORCE): FacingOurRisk.org
- Bright Pink: BrightPink.org
- American Cancer Society®: Cancer.org

Quest Advanced Oncology®: supporting you and your patients **throughout their journey**

The more you know about your patient's risk of hereditary cancer, the better you can navigate the next steps together. As one of the world'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.

Trust Quest Diagnostics for all of your cancer testing needs. We offer the broadest menu available across the continuum of cancer care, and the expertise that comes from more than 20 million oncology tests per year.

To learn more about Quest Diagnostics, visit QuestHereditaryCancer.com or call Quest Genomics Client Services at **1.866.GENE.INFO (1.866.436.3463)** to speak with a genetic counselor.

Test codes may vary by location. Please contact your local laboratory for more information.

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QuestDiagnostics.com