INVITAE

Genetic testing for hereditary cancer

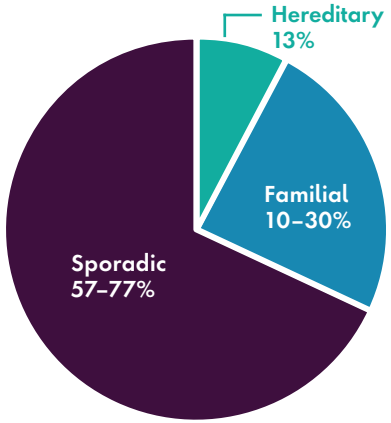
The genetics of hereditary cancer

About half of all men and one-third of all women in the US will develop cancer during their lifetimes.

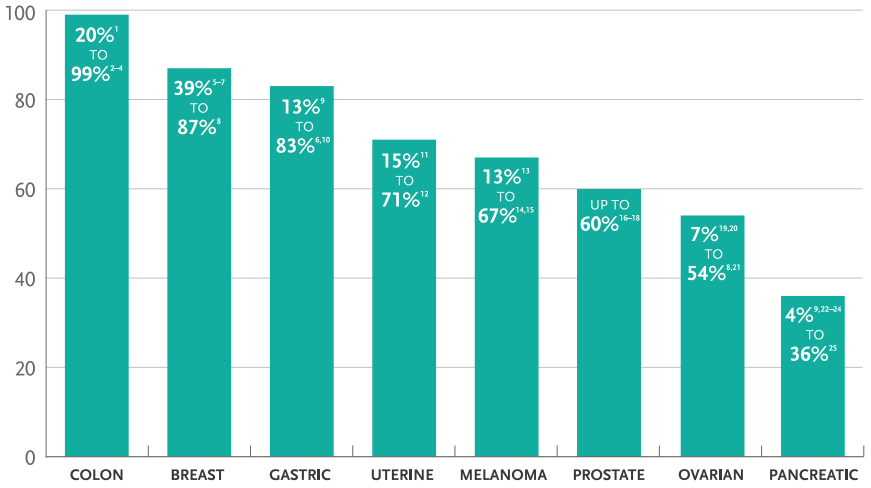
Approximately 13% of all cancers are hereditary. An additional 10% to 30% have a close family member who also had cancer, suggesting a familial link even though no specific hereditary link was found. And 57% to 77% of cancer patients have what's called sporadic cancer, meaning the cancer does not seem connected to inherited genetic traits, or is the result of many different factors.

In **hereditary cancer**, an increased risk of developing certain cancers is passed down through families via their genes.

The past few decades have seen incredible advances in genetic knowledge, and we have now identified many genes associated with cancer. If you have an alteration in one of these genes, your risk of developing certain types of cancer is significantly higher than that of the general population.



Lifetime cancer risk for people with a genetic alteration



Who should consider genetic testing?

Genetic testing may be appropriate if:

- You or a relative* have had a rare cancer (e.g., ovarian, pancreatic, male breast, metastatic prostate, triple negative breast, medullary thyroid)
- You or a relative have had an early onset cancer (e.g., colorectal, endometrial (uterine), or breast cancer diagnosed prior to age 50)
- You or a relative have been diagnosed with two different cancers; this might be cancer in two different areas of the body (e.g., a colon and a uterine cancer) or two separate cancers in the same organ (e.g., bilateral breast cancer)
- There are multiple relatives on the same side of your family with the same or associated types of cancer (e.g., breast/ovarian/pancreatic/prostate or colorectal/endometrial [uterine]/gastric [stomach]/ovarian/pancreatic)
- You have had 10 or more colorectal polyps found during your colonoscopies
- You have Ashkenazi Jewish ancestry on either side of your family
- You have a relative who tested positive for a genetic variant related to cancer risk

**Relatives to consider include siblings, children, parents, aunts, uncles, and grandparents.*

What are the benefits of genetic testing?

Knowing if you have an inherited risk empowers you to be proactive about your health.

Increased surveillance can identify a cancer at its earliest, most treatable stage.

If desired, surgery can significantly reduce risk.

Certain medicines can prevent cancer from developing ("chemoprevention").

Genetic information can qualify you for participation in clinical trials or research studies.

Based on your specific medical history and information about family members diagnosed with cancer, you and your healthcare provider might choose one of these genetic tests—or personalize one of these tests for your unique situation.

	GENES	BREAST & GYN	ENDOCRINE	GASTROINTESTINAL	GENITOURINARY	HEMATOLOGIC	NERVOUS SYSTEM/BRAIN	PROSTATE	SARCOMA	SKIN
INVITAE BREAST CANCER GUIDELINES-BASED PANEL	ATM	✔		✔				✔		
INVITAE BREAST CANCER STAT PANEL	BRCA1	✔		✔	✔			✔		
	BRCA2	✔		✔	✔			✔		✔
	CDH1	✔		✔						
	CHEK2	✔	✔	✔				✔		
	PALB2	✔		✔						
	PTEN	✔	✔	✔	✔		✔			✔
	STK11	✔		✔	✔					
	TP53	✔	✔	✔	✔	✔	✔	✔	✔	✔
INVITAE COMMON HEREDITARY CANCERS PANEL	BARD1	✔								
	NF1	✔	✔	✔			✔			
	APC		✔	✔			✔		✔	
	AXIN2			✔						
	BMPR1A			✔						
	BRIP1	✔								
	CDK4									✔
	CDKN2A			✔						✔
	CTNNA1			✔						
	DICER1	✔	✔		✔		✔		✔	
	EPCAM	✔		✔	✔		✔			
	GREM1			✔						
	HOXB13									
	KIT			✔					✔	
	MEN1		✔	✔			✔			
	MLH1	✔		✔	✔		✔	✔		
	MSH2	✔		✔	✔		✔	✔		
	MSH3			✔						
	MSH6	✔		✔			✔			
	MUTYH			✔						
	NBN*									
	NTHL1			✔						
	PDGFRA			✔					✔	
	PMS2	✔		✔	✔		✔	✔		
	POLD1			✔						
	POLE			✔						
	RAD50*									
	RAD51C	✔								
	RAD51D	✔								
	SDHA		✔	✔			✔		✔	
	SDHB		✔	✔	✔		✔		✔	
	SDHC		✔	✔	✔		✔		✔	
	SDHD		✔	✔			✔		✔	
	SMAD4			✔						
	SMARCA4	✔					✔			
	TSC1			✔	✔		✔			
	TSC2			✔	✔		✔			
	VHL		✔	✔	✔		✔			

*Alterations in RAD50 and NBN are not clearly associated with an increased risk for cancer; however, they may qualify certain patients for clinical trials.

What can genetic testing tell me?

A POSITIVE TEST RESULT CAN:

- Pinpoint your risk of developing cancer, enabling you to make informed medical decisions to reduce risk
- Provide an explanation for your personal or family history of cancer
- Identify other at-risk relatives for whom genetic testing is recommended

A NEGATIVE TEST RESULT:

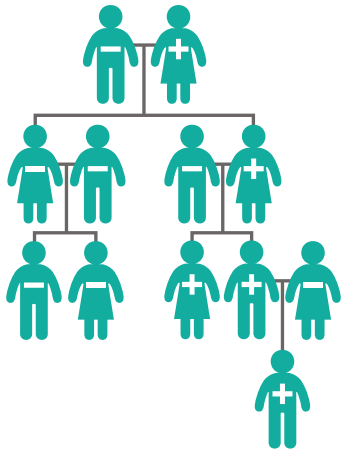
- Means that you do not have an alteration in the genes tested
- Your overall cancer risk depends on your medical history, family history, and environment

AN UNCERTAIN VARIANT TEST RESULT:

- Means that an alteration was identified, but it is not currently known if that alteration increases risk
- Should not be used to guide your medical care
- Invitae will update your healthcare provider if new information becomes available

What can genetic testing do for my family?

Identifying at-risk family members is one of the most important benefits of genetic testing. If you have a genetic alteration, your immediate family members could have a 50% chance of having the same alteration. Other relatives may also be at risk.



Invitae is dedicated to ensuring that both you and your family know your risk. **If you receive a positive test result from Invitae, we can test your blood relatives for that same alteration under our family variant testing program.** Learn more at www.invitae.com/patients/family-testing.

Next steps

- ☐ Submit a saliva or blood sample for testing.
  - Your sample was submitted on _____
- ☐ After receiving your sample, Invitae will send results to your healthcare provider in 10–21 calendar days on average for standard orders and 5–12 calendar days for STAT panels.
- ☐ Learn more about genetic testing, including potential results and suggestions for how to talk with your family, at www.invitae.com/patients.

Have questions? Talk with a genetic counselor

- If you're not working with one, Invitae can help you find a local genetic counselor. Our experienced, board-certified genetic counselors are also available by telephone to answer your questions. Simply call 800-436-3037 and ask to speak with a genetic counselor.
- Invitae also offers a comprehensive post-test genetic counseling session at no additional charge. During this session, our experienced genetic counselors will review your personal and family medical history, and discuss what your genetic test results mean for you and your family. To schedule a post-test genetic counseling session, please call 800-436-3037.

About Invitae

Invitae is a different type of genetic testing lab. Our mission is to bring genetic information into healthcare providers' offices to improve the quality of healthcare.

To do that, we're dedicated to making genetic testing affordable and accessible:

- Invitae bills insurance less than most other labs, which means a lower out-of-pocket cost for you.
- If your insurance company charges you more than $100, Invitae offers payment options and a financial assistance program. Call us at 800-436-3037.
- Invitae works with all insurance companies, including Medicare and Medicaid.
- If you don't have insurance or prefer not to bill your insurance, you have the option to pay $250 for your hereditary cancer genetic testing. Just tell your healthcare provider that you would like to take advantage of Invitae's patient-pay option. Invitae will send you a link to pay online via credit card.

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This guide applies only to gene and panel testing; for exome testing please see the Invitae exome patient guide.