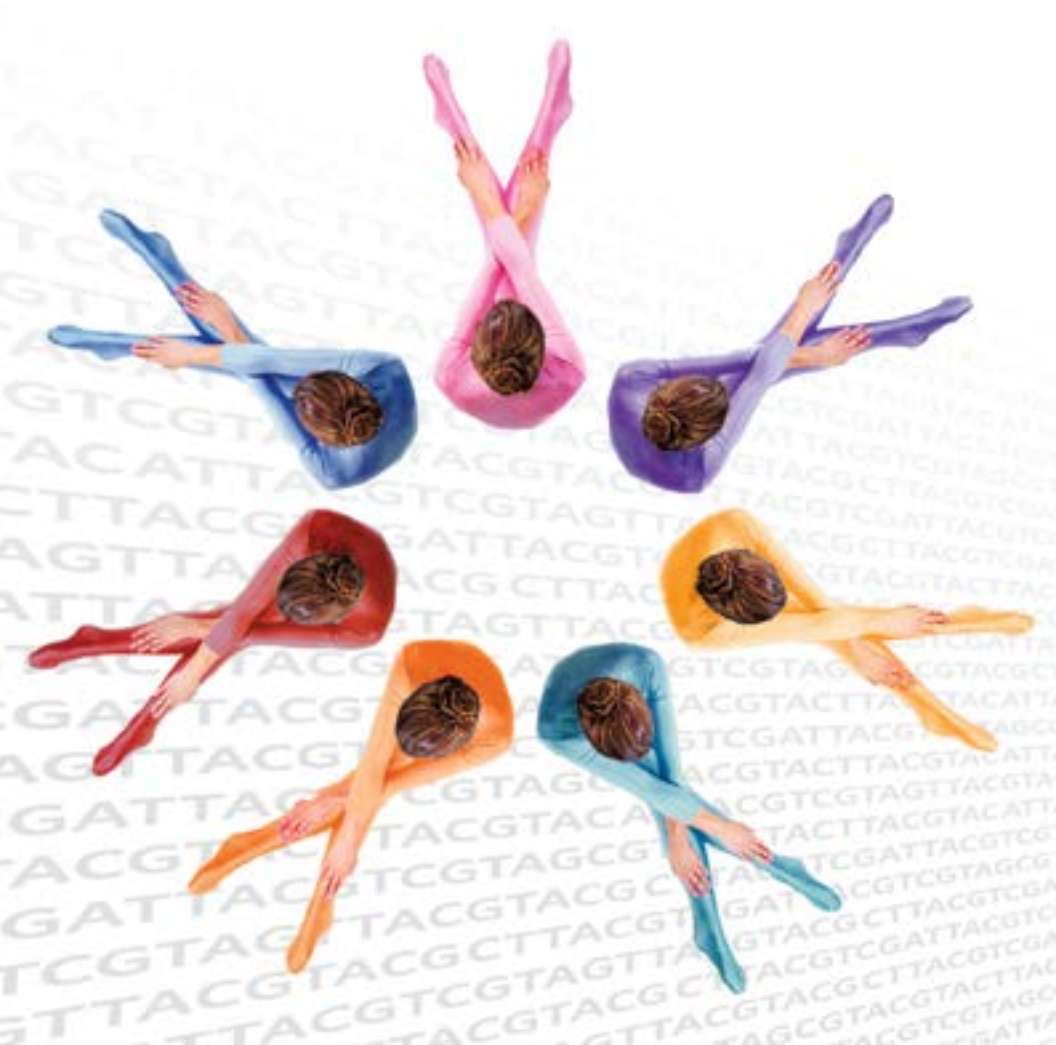
Ambry Genetics®

CancerNext-*Expanded*

Genetic testing for hereditary cancer

PATIENT GUIDE

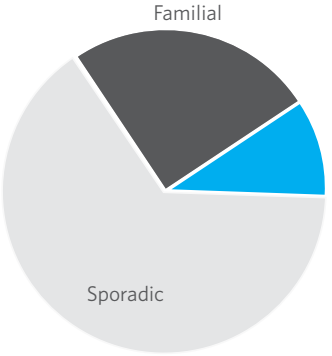


What is Hereditary Cancer?

Cancer affects many people in the U.S. (about 1 in 3 people will develop cancer during their lifetime). There are more than 100 different types of cancer. The majority of cancer occurs at older ages, in people with little or no family history of the disease and no genetic risk. These occurrences are called "*sporadic*" cancers and happen by chance.

Although many people have a family history of cancer, the majority of cancer is not due to inherited causes. Only about 10% of cancer is "*hereditary*" (due to inherited genetic changes called mutations). People who carry these mutations are born with them – they do not develop over time. Understanding if cancer is due to an inherited mutation can help clarify future risks to develop cancer, and help determine options for cancer screening and prevention.

CANCER TYPE BREAKDOWN



There are many different genes known to cause hereditary cancer. These genes increase risk for specific cancers, and there are many genes known for each cancer type.

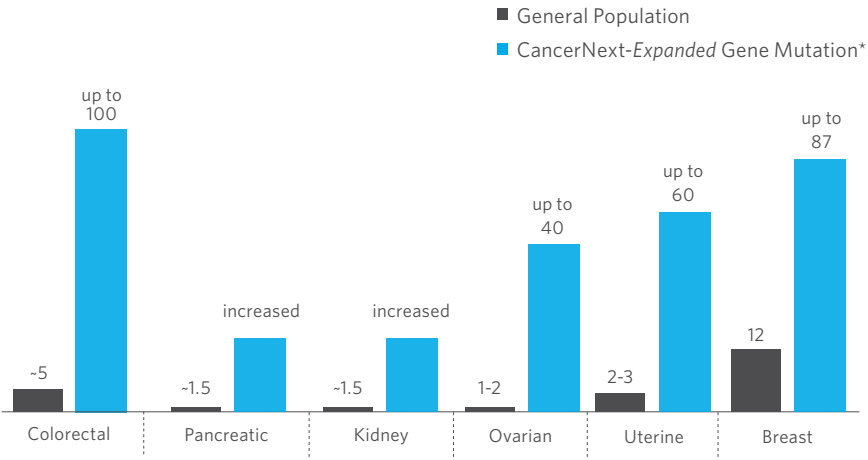
Many families with a history of cancer do not have an identifiable genetic cause. These "*familial*" cases may be due to other genes, shared factors such as environment and lifestyle, or a combination of all of these.

What is Your Risk for Cancer?

A healthcare provider can help you learn about your chance of developing cancer.

- A person with no family history of cancer is most likely at average risk (shown on graph below as general population risk).
- For the person who has a family history of cancer, genetic testing may help determine his/her risk of developing cancer.
- If a person has had cancer, genetic testing may to help determine if he/she has an increased risk for additional cancers.
- Defining a person's risk for cancer helps his/her healthcare providers make personalized recommendations for cancer screening and prevention.

LIFETIME CANCER RISKS FOR COMMON CANCERS (%)



*Mutations in most genes included in CancerNext-*Expanded* lead to an increased risk for some common cancers in this graph, but not all. This graph represents the highest risks associated with some genes in CancerNext-*Expanded*.

Is Hereditary Cancer Testing Appropriate for You?

Genetic testing may be appropriate if you have a personal history and/or family history of any of the following:

- ☐ More than one cancer in the same person (like colorectal and breast cancer or ovarian and thyroid cancer)
- ☐ Multiple close family members with cancers diagnosed younger than age 50*
- ☐ 3 or more close family members with different types of cancer*
- ☐ Families with previous cancer genetic testing and but no mutation found
- ☐ Rare cancers at any age (like paraganglioma, pheochromocytoma, or medullary thyroid cancer)

*On the same side of the family

CancerNext-*Expanded* Genes and Associated Cancer(s)

GENE(S)	ASSOCIATED CANCER(S)/TUMOR(S)
AIP	Pituitary adenoma
ALK	Nerve tumors, possibly medulloblastoma
APC	Colorectal, pancreatic, medulloblastoma, other
ATM	Breast, pancreatic , prostate
BAP1	Kidney, melanoma, mesothelioma
BARD1, MRE11A, RAD50	Breast, possibly ovarian
BLM	Breast, colorectal
BRCA1, BRCA2	Breast, ovarian, male breast, prostate, pancreatic
BRIP1, RAD51C, RAD51D	Breast, ovarian
BMPR1A, SMAD4	Colorectal, stomach, pancreatic
CDH1	Breast, gastric, colorectal
CDK4	Melanoma
CDKN1B	Hyperparathyroidism, pituitary adenoma, other

Continued: CancerNext-*Expanded* Genes and Associated Cancer(s)

GENE(S)	ASSOCIATED CANCER(S)/TUMOR(S)
CDKN2A	Melanoma, pancreatic, astrocytoma
CHEK2	Breast, colorectal, prostate, other
DICER1	Pleuropulmonary blastoma, cystic nephroma, brain, other
FANCC	Breast, possibly pancreatic
FH	Kidney, PGL/PCC, leiomyomas
FLCN	Kidney
GALNT12	Colorectal
GREM1	Colorectal
HOXB13	Prostate
MAX	PCC
MEN1	Parathyroid, GEP tumors, pituitary adenoma, adrenal, other
MET	Kidney
MITF	Kidney, melanoma
MLH1, MSH2, MSH6, PMS2, EPCAM	Colorectal, uterine, stomach, ovarian, glioma, prostate, other
MUTYH	Breast, colorectal
NBN	Breast, possibly ovarian, brain, prostate
NF1	Female breast, malignant nerve sheath tumors, optic glioma, astrocytoma, other
NF2	Vestibular schwannomas, other schwannomas, meningiomas, spinal tumors
PALB2	Breast, ovarian, pancreatic, male breast, possibly prostate
PHOX2B	Nerve tumors

PGL: Paraganglioma
PCC:Pheochromocytoma

GEP tumors: gastro-entero-pancreatic tumors. These include gastrinomas, insulinomas, vasoactive intestinal peptide-secreting tumors (VIPomas), and glucagonomas.

GENE(S)	ASSOCIATED CANCER(S)/TUMOR(S)
POLD1, POLE	Colorectal
POT1	Gliomas
PRKAR1A	Primary pigmented nodular adrenocortical disease, pituitary adenoma, myxomas, thyroid nodules, schwannomas, other
PTCH1	Basal cell carcinomas, medulloblastoma, sarcoma, other
PTEN	Breast, uterine, kidney, thyroid, colorectal
RB1	Retinoblastoma (childhood), melanoma, sarcoma
RET	Thyroid (medullary), PCC
SDHA, SDHAF2, SDHB, SDHC, SDHD	PGL/PCC, kidney, GIST
SMARCA4	Ovarian, brain, other
SMARCB1	Atypical teratoid/rhabdoid tumors of nervous system/ kidney, schwannomatosis, other
SMARCE1	Meningioma
STK11	Small bowel, colorectal, pancreatic, breast, ovarian
SUFU	Basal cell carcinomas, jaw keratocysts, medulloblastoma, other
TMEM127	PGL/PCC
TP53	Breast, sarcoma, brain, adrenocortical, leukemia, and others
TSC1, TSC2	Kidney, brain and spine, skin, liver, lung, heart
VHL	Kidney, hemangioblastomas (brain and spine), other
XRCC2	Female breast, male breast

PCC: Pheochromocytoma
PGL: Paraganglioma
GIST: Gastrointestinal stromal tumor

Possible Genetic Test Results

If you or your family member has genetic testing, you will receive one of three possible results:

RESULTS	EXPLANATION
Positive	• A mutation was found in one of the genes tested • Increased risk for cancer specific to the gene that has a mutation • Gene-specific cancer screening and prevention recommendations • Offering genetic testing to adult at-risk relatives for the specific mutation is recommended
Negative	• No changes, or mutations, were found in any of the genes tested • Cancer risk(s) are based on personal and family history • Cancer screening and prevention recommendations based on family history • Genetic testing most likely will not be appropriate for family members
Variant of Unknown Significance (VUS)	• A genetic change was found, but it is unclear if this change causes an increased risk for cancer or not • Cancer risk(s) are specific to the family history of cancer • Cancer screening and prevention recommendations based on family history • Family studies may be helpful

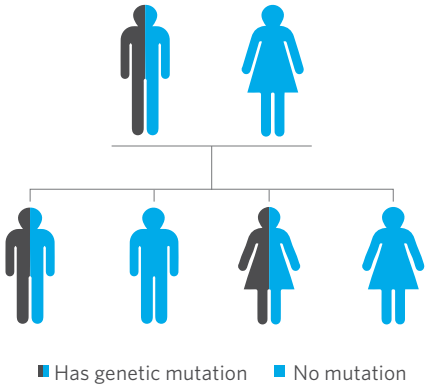
NOTES

If You Test Positive for a Gene Mutation

- Cancer screening will most likely begin in young adulthood
- Screening will be recommended for cancers specific to the gene in which the mutation was found
- Cancer prevention options will be discussed
- Family members may be tested to find out if they carry the same mutation

What This Means for a Family

There is a 50/50 random chance to pass on a genetic mutation in a CancerNext-*Expanded* gene to your sons and daughters. The image below shows that both men and women can carry and pass on these mutations. Most inherited cancer syndromes occur when a gene mutation is inherited from a mother or father. However mutations in some of these genes (*SDHD, MAX, SDHAF2*) are more likely to increase your risk of tumors/cancer if a father passes it on. If a mother passes this gene mutation on to you, you will likely not be at increased risk, but you could pass the mutation on to your children. Typically, *MUTYH*-associated polyposis occurs when a mutation in *MUTYH* is inherited from both parents.



Test Result and Recommendations

To be completed by you and your healthcare provider when you receive your genetic test results and medical management recommendations

TEST RESULT

☐ No mutation detected

☐ Positive for a mutation in _____ gene

☐ Variant of unknown significance in _____ gene

RECOMMENDATIONS FOR YOU

RECOMMENDATIONS FOR FAMILY MEMBERS

☐ Genetic testing not appropriate for family members

☐ Genetic testing recommended for family members

FAQs about Billing and Insurance

Q1. WHAT IS AMBRY'S BILLING POLICY?

Ambry offers a variety of payment options. Many insurance plans cover genetic testing and Ambry is contracted with the majority of U.S. health plans. Your out-of-pocket cost may vary based on your individual plan. We offer personalized verification of insurance coverage and financial options for your genetic testing. A team of dedicated specialists is available to help you get access to the genetic testing you need and answer any questions you have about our payment options. Call or email our Billing department at +1-949-900-5795 or billing@ambrygen.com with any questions.

Q2. WHAT IS AN EXPLANATION OF BENEFITS (EOB)?

It is not a bill and does not require payment. Your insurance company sends you an EOB to explain any services paid on your behalf. You can contact us directly to speak with a Billing specialist with any questions/concerns about your EOB. Some genetic tests take weeks to process to receive the best results. In addition, insurance companies can take over two months to process claims, and longer if we need to send information again, and this could delay your bill.

Q3. HOW MUCH DO AMBRY'S TESTS COST?

We are committed to making the genetic testing process as simple and cost-effective as possible. Prices depend on if your insurance plan is contracted with Ambry, and if they are a private or public plan. We also offer prices when someone pays by cash, or when an institution pays. This is not necessarily what is reflected on an EOB, so please contact us directly to speak with a Billing specialist with any questions/concerns.

Q4. WHY DID I RECEIVE A BILL MORE THAN A MONTH AFTER MY TEST?

Some genetic tests take weeks to process to receive the best results. In addition, insurance companies can take over two months to process claims, and longer if we need to send information again. All of this could delay your bill, but we try our best to prevent this from happening.

Resources for Patients

These and other resources can help build a sense of community and aid in answering some common questions.

AMBRY'S HEREDITARY CANCER SITE FOR FAMILIES
patients.ambrygen.com/cancer

BRIGHT PINK
brightpink.org

FACING OUR RISK OF CANCER EMPOWERED (FORCE)
facingourrisk.org

HEREDITARY COLON CANCER FOUNDATION
hcctakesguts.org

THE VHL ALLIANCE
vhl.org

LI-FRAUMENI SYNDROME ASSOCIATION
lfsassociation.org

GENETIC INFORMATION NONDISCRIMINATION ACT INFORMATION
ginahelp.org

Find a Genetic Counselor

NATIONAL SOCIETY OF GENETIC COUNSELORS
nsgc.org

CANADIAN ASSOCIATION OF GENETIC COUNSELLORS
cagc-accg.ca

About Ambry

Ambry is a genetics-based healthcare company that is dedicated to open scientific exchange so we can work together to understand and treat all human disease faster.

AMBRY GENETICS

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