Rare Disease

Patient Guide

A Guide to Genetic Testing for Rare and Undiagnosed Conditions

Ambry Genetics®
A TEMPUS COMPANY

Understanding The Basics

Genome: The information contained across all ~3 billion DNA base pairs in the nucleus of the cell[1]

WHY IS GENETIC TESTING IMPORTANT?

Our genes carry a story that is unique to us and makes us who we are. Taking a closer look at genes can help health care providers better understand the cause of medical concerns.

- By knowing the underlying genetic cause of a condition, doctors may be able to treat and manage the patient's health better.
- They may also be able to better understand if a medical condition may also affect other family members.
- As researchers and doctors continue to learn more about genomics, we are able to find better treatments and cures for certain conditions.

BENEFITS OF GENETIC TESTING

Comprehensive genetic tests may help find the underlying cause of medical concerns. Finding a diagnosis through this testing is beneficial because it:

- Enables quicker and more cost-effective diagnosis as multiple genes are tested at once.
- May guide or influence treatment or medical health care decisions.
- May remove uncertainty related to having an undiagnosed condition.
- Provides awareness about health concerns in family members and/or risk of passing the genetic change on to future children.

Different types of genomic testing

Genome
Apple

Exome
Slice

Gene Panel
Piece

Genome: Analyzes nearly 100% of the genetic code even the parts that link the ~20,000 genes in the DNA.[2]

Exome: Analyzes the ~20,000 genes that make up the DNA.[3]

GENOME SEQUENCING

The genome is the complete instruction manual for a person. It includes all 20,000 genes and the deep regions that control how those genes behave, providing the most thorough genetic test possible. By reading nearly the complete instruction manual, this test increases the chances of getting an answer.

EXOME SEQUENCING

Exome sequencing is a comprehensive test designed to look for genetic changes (mutations) in genes that may be the cause of an existing medical condition. Some genetic tests just look for common mutations, while others may just look for changes in common genes. Exome sequencing analyzes all genes, making it a comprehensive genetic test.

CHROMOSOMAL MICROARRAY (CMA)

Chromosomal Microarray is a test designed to look for changes in the packages that hold genetic information (genes). CMA is especially good at finding extra or missing pieces of the packages that hold genes. For many people, changes in their genes may be the cause of an existing medical condition.

CHOOSING THE MOST APPROPRIATE TEST

A health care provider may consider genome or exome sequencing and/or CMA to identify the underlying genetic cause of medical concerns when:

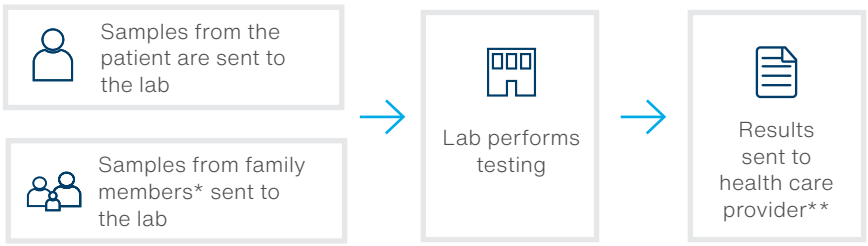
1. Previous genetic and medical tests have not yet found the cause of medical concerns, and a health care provider suspects there may be an underlying genetic cause.
2. There is no specific genetic testing available for the suspected genetic condition.
3. Medical conditions can be caused by changes in more than one gene and genomic testing is a way to test for all of them at once.

The American College of Medical Genetics and Genomics (ACMG) and the Amercian Academy of Pediatrics (AAP) practice guidelines recommend exome and/or genome sequencing as a first-tier or second-tier test for patients with congenital anomalies, developmental delays, and intellectual disabilities.[4-5]

The Testing Process

Testing is performed using a blood or saliva sample, which is collected using a special kit that is shipped overnight to Ambry Genetics, all coordinated by the health care provider. Samples are collected from the patient and close family members (blood relatives).

The health care provider will receive the results; they will not be sent directly to the patient. Every health care provider may have a different method and time frame to contact the patient to discuss results, so it is important to discuss this process with them. Based on the test results, the health care provider will discuss any next steps.



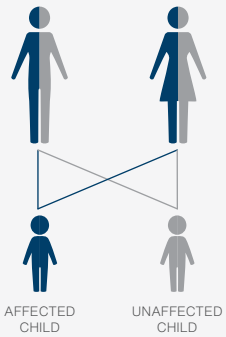
* *"Family members" refers to blood relatives, such as brothers/sisters/parents/grandparents/aunts/uncles/cousins*

** *Results for CMA and exome/genome sequencing are sent to the health care provider. Availability of results will depend on the type of test ordered with some results taking as long as 7 weeks.*

WHY MIGHT THIS TESTING INVOLVE FAMILY MEMBERS?

Genetic testing may provide more accurate answers when the patient's DNA is compared to close relatives such as biological parents, grandparents, and siblings. This helps sort through all the genetic changes and identify those that are common in the family vs. those that may be causing the medical condition in the patient. Or, if multiple people in the family have the same medical condition, it helps to see which of the same genetic changes each family member has.

This testing is still possible without the patient's blood relatives, but it lowers the chance of finding the answer. Family members can submit a blood or saliva sample to participate in testing.



Genetic Testing Results

It is important to discuss results with the health care provider to determine how they will impact medical care.

PRIMARY RESULTS

(+) POSITIVE/LIKELY POSITIVE

An alteration or change was found in the DNA that is known to be associated with the medical concerns.

Genetic testing may be considered for family members.

(?) UNCERTAIN

An alteration or change was found in the DNA, but it is not clear if this is the cause for the medical concerns.

As part of our Patient for Life™ program, we will keep the results on file as future genetic discoveries may provide useful information and will notify the health care provider if any clinically significant alterations are identified.

(–) NEGATIVE

The underlying genetic cause of the medical concerns has not been found.

As part of our Patient for Life program, we will keep the results on file as future genetic discoveries may provide useful information and will notify the health care provider if any clinically significant alterations are identified.

SECONDARY FINDINGS RESULTS (EXOME/GENOME SEQUENCING ONLY)

(+) POSITIVE/LIKELY POSITIVE

A mutation was found in a gene that is unrelated to current medical concerns but may affect the patient's health in the future.

Genetic testing may be considered for family members. It will be important to discuss these findings with the healthcare provider.

(–) NEGATIVE

No mutations were identified among a group of common disease genes unrelated to current medical concerns.

There may still be genetic changes that may affect the patient's future health; however, they were not identified through this test.

Things to Know

In some cases, results may be negative. Although these tests are designed to look at the entire exome/genome, the cause of medical concerns may be in an area of the exome/genome that is not well understood or cannot be identified.

If results are negative, the health care provider may choose to perform additional genetic testing now or in the future. Negative results could also suggest that the medical issues are not inherited.

PATIENT FOR LIFE™ PROGRAM

Scientists are learning more about genes and discovering new insights on how they impact health nearly daily. Ambry Genetics has a unique program where our scientists stay up-to-date with the latest research to see how it could impact a patient's health. As new discoveries are made, our scientists proactively reanalyze all previous patients' data to determine whether they may benefit from this new information. If we find clinically significant information, we will proactively issue an updated result report to the ordering health care provider. This service is offered indefinitely and at no additional cost to the patient.

SECONDARY FINDINGS FOR EXOME/GENOME SEQUENCING

Because this test looks at all the genes at once, medically important mutations may be found that have nothing to do with the current medical concerns. If this happens, you could potentially learn new information about your or your child's health, for which there may be recommended medical follow-up. You can choose ahead of time if you wish to learn about this information.

TESTING FOR FAMILY MEMBERS

Genomic testing may find a genetic change in the patient that may also be found in the patient's family. It is important to consider sharing these results; however, some family members may not want to know if they are at risk for developing a genetic condition. Ideally, family members should meet with their health care provider or a genetic counselor to discuss their options for being tested. Genomic testing may also find unexpected information about family relationships. You can discuss these possibilities with your health care provider and/or genetic counselor.

Ambry offers no-cost testing for all blood relatives in the United States within 90 days of the original patient report.

Frequently Asked Questions

1 HOW IS EXOME/GENOME AND CMA TESTING PERFORMED AND HOW LONG DOES IT TAKE?

Exome/genome and CMA testing are performed using a blood or saliva sample from the patient, which is collected using a special kit that is shipped overnight to Ambry, coordinated by the health care provider. For exome or genome testing, samples are collected from the patient and up to two other close family members. Exome or genome testing can take up to 7 weeks while CMA testing takes about 2-3 weeks for the testing to be completed. Results are sent to the health care provider.

2 WHAT WILL HAPPEN WHEN RESULTS ARE READY?

The health care provider will receive the results; they will not be sent directly to the patient. Every health care provider may have a different method and time frame to contact you to discuss results, so it is important to discuss this process with them. Based on the test results, the health care provider will discuss any next steps.

3 WILL GENOMIC TESTING BE COVERED BY INSURANCE?

Many insurance plans cover genetic testing and Ambry is contracted with the majority of U.S. health plans. The out-of-pocket cost may vary based on the individual plan. Ambry offers personalized verification of insurance coverage and financial options for genetic testing. A team of dedicated specialists is available to help get access to the genetic testing needed and answer any questions about our payment options. Call or email our billing department at +1.949.900.5795 or billing@ambrygen.com with any questions.

4 WHAT IS AN EXPLANATION OF BENEFITS (EOB)?

The insurance company sends the patient an EOB to explain any services paid on the patient's behalf. This is not a bill. The patient or the responsible party can contact Ambry directly to speak with a billing specialist with any questions or concerns about the EOB. Some genetic tests take weeks or months to process in order to receive the best results. In addition, insurance companies can take several weeks or even a couple of months to process claims.

5 WILL THE GENOMIC TEST RESULTS AFFECT INSURANCE COVERAGE?

In the U.S., the Genetic Information Nondiscrimination Act (2008) prohibits discrimination by health insurance companies and employers based on genetic information. Visit ginahelp.org to learn more.

6 WHAT IF I DO NOT HAVE INSURANCE?

Ambry Genetics offers self-pay pricing and a Patient Assistance Program for patients who do not have health insurance or whose insurance does not cover exome or genome testing. For more information, please contact our billing department at +1.949.900.5795 or billing@ambrygen.com with any questions.

STILL HAVE QUESTIONS?

Talk to your health care provider or visit our website: ambrygen.com

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MKT-SPEC-BRO-50024-EN v5 06.04.26

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