ExomeNext®
PATIENT GUIDE

Rare Disease

Patient Guide

A Guide to Genetic Testing for Rare and Undiagnosed Conditions

Ambry Genetics® | LifeStrands

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.

What are the different types of genomic testing?

BENEFITS OF GENETIC TESTING

Genome
Apple

Exome
Slice

Gene Panel
Piece

Exome: ~1% of the genome that codes for proteins. This accounts for ~20,000 genes.[2]

>60% of all known diseases are caused by changes in the exome.[3]

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 your genes. For many people, changes in their genes may be the cause of an existing medical condition.

IS EXOME SEQUENCING OR CMA RIGHT FOR YOU?

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

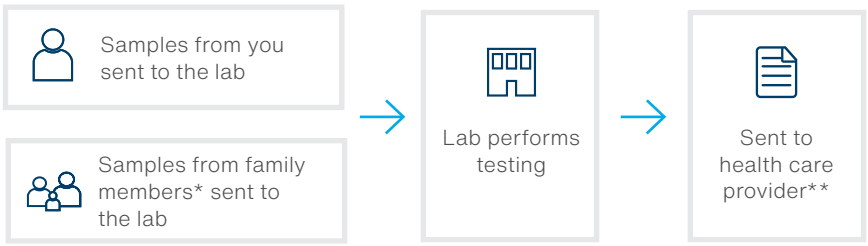
1. Previous genetic and medical tests have not yet found the cause of medical concerns, and a health care provider suspects there may be an underlying genetic cause.
2. There is no specific genetic testing available for the suspected genetic condition.
3. Medical conditions can be caused by changes in 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) 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]

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.



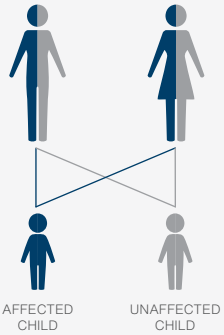
* *"Family members" refers to blood relatives, such as brothers/sisters/parents/grandparents/aunts/uncles/cousins*

** *Results for CMA and exome sequencing are sent to the health care provider in 2-3 weeks and 6-8 weeks, respectively.*

WHY MIGHT THIS TESTING INVOLVE FAMILY MEMBERS?

Exome sequencing 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 for the specific alteration 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 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 for the specific gene mutation may be considered for family members. It will be important to discuss these findings with your or your child's doctor.

(–) 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 you are concerned about 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 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 within 90 days of the original patient report. Family testing is done via specific site analysis for pathogenic or likely pathogenic variants.

Frequently Asked Questions

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

Exome 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 testing, samples are collected from the patient and up to two other close family members. Exome testing takes about 6-8 weeks while CMA testing takes about 2-3 weeks for the testing to be completed and results are sent to the health care provider.

2 WHAT WILL HAPPEN WHEN MY 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.

STILL HAVE QUESTIONS?

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

Ambry Genetics, a subsidiary of REALM IDx, Inc., excels at translating scientific research into clinically actionable test results based on a deep understanding of the human genome and the biology behind genetic disease. Ambry has an unparalleled track record of discoveries over 20 years and a database that continually expands through collaboration with academic, corporate, and pharmaceutical partners. Being first to market with innovative products and comprehensive analysis, Ambry enables clinicians to confidently inform patient health decisions. For more information, please visit ambrygen.com.

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