Exome Sequencing

A Guide for Patients

GeneDx
an OPKO Health Company
What is an exome?

Altogether, the exons in our body make up our exome and all the genes (exons and introns) make up our genome. So our exome is the group of all the pieces of DNA that tell our bodies how to make proteins.

Genetics Glossary:

**Proteins** are the building blocks that make our body work. They make up our muscles, skin, hormones, and many other chemicals that allow our bodies to function.

**DNA** is the instruction book that tells our bodies how to make the proteins.

**Genes** are the chapters of the instruction book and are made of two types of pieces:

- **Exons** are the pieces that come together to make proteins.
- **Introns** are regions between exons that are cut out when proteins are made.
What is XomeDx®?

XomeDx is GeneDx’s test to read and check the spelling of the exome by a method called sequencing. Exome sequencing is currently one of the most comprehensive genetic tests available.

How is XomeDx testing done?

Your blood or saliva sample is sent to our laboratory.

Our lab takes your DNA from your sample.

We use special tools to read your exome and compare it to our database. During this comparison, we look for typos in the “spelling” of your DNA, also known as genetic variants.

Our experts review the variants to see if they may change the way the protein works in your body and if the change may be the cause of your symptoms or features.
How will I get the results?

XomeDx can take a few months for the lab to complete. A report that explains your results will be sent to your healthcare provider who ordered your testing.

What type of results can I expect?

There are three types of results from XomeDx. Your test report may contain a table with one or more of the three types listed below:

Pathogenic or Likely Pathogenic Variant

A "typo" or change in DNA that is very likely to cause your features and symptoms. This is the most straightforward result and can be used to test other family members to see their chance of having the disease or having a child with the disease.

Variant of Uncertain Significance (VUS)

A change in a gene, but we are not sure if it is the cause of your symptoms/features. More information is needed to know if the variant is the cause of your symptoms or not. We may suggest testing other members of your family to help figure out the meaning of the result.

Negative

We did not find any variants that could explain your symptoms in any part of your exome that we tested. This does not mean that you do not have a genetic condition. It is still possible that there is a genetic variant that was not found by this test. Your doctor or genetic counselor may discuss additional testing now or in the future.

Is other genetic information included in the report?

The American College of Medical Genetics and Genomics (ACMG) recommends that we report any secondary findings found on exome sequencing. Secondary findings are not related to your current symptoms, but may give useful health information. For example, the lab may find a genetic change that increases the risk for cancer or increases the risk of a heart condition. This secondary information may be used by both you and your family. All secondary findings will be included in your report, unless the opt-out checkbox is checked on the consent form.
Can XomeDx find all possible genetic causes of disease?

XomeDx does not find all possible causes of genetic disease. Some types of variants and any variant outside of the exome cannot be found by this test. Other types of testing may be needed. Please speak with your doctor about the best testing options for you and your family.

Why does GeneDx need to test other family members?

When doing exome sequencing, it is best to compare the patient’s DNA with two or more family members to form a “trio”. Biological parents of the patient are best, if available, as they give us the most information. Trio testing greatly improves the chance of finding the correct variant and decreases the chance of finding a VUS. If the biological parents are not available and there are no other people in the family with the same symptoms, please have your healthcare provider contact GeneDx to see which family members are best to include.

If you are testing multiple people in a “trio”, why is there only one report?

The samples from the other family members are only used to compare to the patient’s DNA. Additional testing that includes a report for other family members can be ordered, for an additional fee.
Should I have genetic counseling before getting this test?

Meeting with a genetic counselor can be very helpful both before and after genetic testing. A genetic counselor can help you and your family understand the benefits and limitations of the test, so you can decide if XomeDx is the best test for you and/or your family. Genetic counseling may also be required by your health insurance company. You can find a genetic counselor near you through The National Society of Genetic Counselors (www.nsgc.org). MyGeneTeam, LLC, a GeneDx preferred partner, offers genetic counseling by phone or online video-conferencing. Get more information about MyGeneTeam at www.mygeneteam.com.

Does GeneDx test family members?

Yes, we offer targeted testing for family members of those found to have a pathogenic or likely pathogenic variant at GeneDx. There is a fee for each family member tested, but it is much less than the cost of additional XomeDx tests for each family member. Targeted testing can also be used for prenatal testing. For more information, please call one of our genetic counselors at 1-888-729-1206.

Should I repeat exome testing in the future?

If your testing did not find a clear answer for your medical condition, your healthcare provider may suggest doing the test again in a few years. As research finds new genes and causes for genetic diseases, future exome testing may show a result that was not known at the time of your first testing.
Will insurance cover this test?
GeneDx accepts most commercial insurance plans. We will contact your health insurance provider to ask for an estimate of your financial responsibility. This is an estimate of your out-of-pocket cost for the testing, given to us by your insurance provider, and it is based on your specific insurance plan and usage. GeneDx offers a no-interest payment plan and has a Financial Assistance Program for eligible patients. For more information, please contact our Benefits Team at benefits@genedx.com or 1-844-241-1233.

What if I do not have insurance?
GeneDx offers self-pay pricing and payment plans for patients who do not have health insurance. For more information, please contact our Benefits Team at benefits@genedx.com or 1-844-241-1233.

Can health insurers or employers discriminate based on genetic test results?
No, the Genetic Information Nondiscrimination Act of 2008, also referred to as GINA, is a federal law that protects Americans from discrimination by health insurance companies and employers based on their genetic information. However, this law does not cover life insurance, disability insurance, or long-term care insurance. For more information, please visit www.genome.gov/10002328.

Where can patients find more information?
More information is available at the following websites:
- National Society of Genetic Counselors, an organization that can help you find a counselor near you: www.nsgc.org
- MyGeneTeam: www.mygeneteam.com
About GeneDx

GeneDx, Inc. is a wholly owned subsidiary of BioReference Laboratories, Inc. an OPKO Health Company. We were founded in 2000 by two scientists from the National Institutes of Health (NIH) to address the needs of patients diagnosed with rare disorders and the clinicians treating these conditions. Today, GeneDx has grown into a global industry leader in genomics, having provided testing to patients and their families in over 55 countries. Led by its world-renowned whole exome sequencing program, and an unparalleled comprehensive genetic testing menu, GeneDx has a continued expertise in rare and ultra-rare disorders. GeneDx also offers a number of other genetic testing services, including: diagnostic testing for hereditary cancers, cardiac, mitochondrial, and neurological disorders, prenatal diagnostics, and targeted variant testing.