485F Route 1 South
Iselin, NJ, 08830
732-652-8000

Whole Exome Sequencing Test

The purpose of whole exome sequencing is to identify a genetic condition in the individual being tested. This consent form provides information about whole exome sequencing, including the possible results, risks, and benefits.

Test Background

DNA provides instructions that tell our body how to grow and function. The DNA in our body is packaged into thousands of genes, which have different functions. Whole exome sequencing looks for changes in these genes. These changes are called variants. Genetic variants are responsible for the differences we see in people, such as hair color or blood type. In some cases, a genetic variant impacts the normal way a gene functions and can cause a disease. These diseases are known as genetic conditions.

The purpose of this test is to see if I, or my child, has a harmful genetic change that could cause a genetic condition or put me, or my child, at risk to develop a genetic condition in the future.

During whole exome sequencing, samples from additional family members (usually the biological parents) may be submitted along with my, or my child's sample. Samples from family members can help the laboratory to interpret the results of this test. If family members are tested, they will not receive a separate report, but relevant information may be included on the report of the individual being tested.

Test Results and Interpretation

The following are the possible types of results I, or my child, may receive from this test:

1. **Positive:** A positive test result means that a genetic variant or multiple genetic variants were identified that are associated with a genetic condition or increased risk to develop a genetic condition. These results may explain my, or my child's, clinical features. These results may have implications for other family members.
2. **Negative:** A negative result indicates that no genetic variants explaining my, or my child's, clinical features were identified. It does not guarantee that I, or my child, does not have a genetic condition or another medical condition. A negative result may be uninformative and may not remove the need for additional testing.
3. **Inconclusive**: An inconclusive result indicates that a variant of uncertain significance has been identified. This means that there is not enough information available to determine if the variant identified causes disease or is a benign change. Testing of additional family members or preforming additional clinical testing can sometimes help to clarify an inconclusive result. In the future, if more information becomes available, an inconclusive result may be reclassified to either a positive or negative result. Your healthcare provider can contact the laboratory to determine if there have been any changes to an inconclusive result.
4. **Unexpected Results (Incidental Findings):** In rare cases, this test may uncover a genetic variant that is important, but not directly related to the reason this test was ordered. This is called an "incidental finding". This information may be returned to the health care provider who ordered the test if it is likely to impact my, or my child's, medical care.

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Test Limitations and Risks

- Whole exome sequencing does not look at all of an individual's DNA sequence. It involves sequencing the coding regions of genes, which are called the "exons". This makes up around 1-2% of an individual's DNA sequence. Variants that exist outside of these regions are not detected. In addition, some exons may not be completely covered by this test.
- This testing may not always give a definitive answer. In certain cases, testing may not identify a genetic variant even though one exists due to limitations in current medical knowledge or the testing technology. In addition, certain types of genetic variants may not be detectable by this test (e.g. large copy number variations, methylation abnormalities, mutations in genes with highly homology, and trinucleotide repeat expansions).
- Although whole exome sequencing is very accurate, rarely inaccurate results may occur. Reasons for inaccurate results include, but are not limited to mislabeled specimens, inaccurate reporting of clinical information or family relationships, rare technical errors, or unusual circumstances such as bone marrow transplantation or mosaicism.
- The interpretation of results is based on the information available in the medical literature and scientific databases at the time of testing. This information is constantly changing. As new information becomes available it may result in a change in the interpretation of these results. Your healthcare provider can contact the laboratory at any time to discuss the current interpretation of a variant or report.
- This test does not have the ability to determine all of long-term medical risks that the patient might encounter. The result of this test does not guarantee patient's or family members' health. Other diagnostic tests may still need to be performed.
- There is a possibility that as part of testing process, biological relationships within a family that do not align with what was reported to the laboratory may be identified. Examples include misattributed paternity (the stated father of an individual is not the biological father) and consanguinity (the parents of an individual are related by blood). In that scenario, it may be necessary for the laboratory to contact the healthcare provider who ordered the testing.

Genetic Counseling

Genetic testing results can be complicated. It is recommended that I receive genetic counseling before and after this test to help me understand the results and limitations of this test. Genetic counseling can be performed by a genetic counselor or a physician. To find genetic counselor in your area visit: https://www.nsgc.org/page/find-a-genetic-counselor.

Patient Confidentiality

My, or my child's, data and personal information will be stored and protected in strict confidence compliant with regulatory requirements. To maintain confidentiality, the test results will only be released to the health care provider who ordered the testing, to the ordering laboratory, to me, to other health care providers involved in my, or my child's care, or to others as entitled by law. The United States Federal Government has enacted several laws that prohibit discrimination based on genetic test results by health insurance companies and employers. In addition, these laws prohibit unauthorized

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disclosure of this information. These laws do not explicitly prohibit discrimination by life and disability insurance providers. For more information, please visit www.genome.gov/10002077

The laboratory may discuss summaries of genetic test results in scientific presentations, publications, or marketing pieces. No names or personal identifiers will be revealed.

International Specimens

If I, or my child, reside outside the United States, I attest that by providing a sample for testing, I am not knowingly violating any export ban or other legal restriction in the country of my residence.

Sample Retention for Research and Database Participation

DNA samples will only be used for testing that is authorized by the ordering provider. Any leftover DNA will be stored for at least 60 days. Some samples may be maintained indefinitely after all testing has been completed for research or quality management purposes in an effort to advance scientific knowledge. In such a case, all personal identifiers will be removed in a HIPAA compliant manner, and no new results will be returned or shared with me or the ordering provider. I may opt in or out of sample retention for research purposes. Samples from New York State residents will be destroyed within 60 days of testing completion, if I opt out of sample retention.

De-identified medical and genetic information can be useful to scientists and physicians to further our understanding of genetics and medicine. Although sharing of such de-identified information may not directly benefit me or my child at this time, it could be beneficial for patient care and clinical research. Genosity may share this type of information with health care providers, researchers, and knowledge databases. Even though this information is de-identified, there is a risk that I, or my child, could be identified based on the medical and genetic information that is shared.

Any research that results in medical advances, including new products, tests or discoveries, may have potential commercial value and may be developed and owned by the laboratory or collaborating researchers. If any individuals or corporations benefit financially from these studies, no compensation will be provided to me or my family. I can opt-out of specimen storage by checking the box in the signature section below.

Targeted Familial Testing

For cases with positive findings, I understand targeted familial testing, i.e., testing whether other family members also have the variant, is not available from this laboratory. I have option to discuss with my healthcare provider to find another clinical laboratory that offers the targeted testing or order the same test as my child when the medial necessity meets standards.

Secondary Findings

Secondary findings are variants in genes that are not related to an individual's reported clinical features. The American College of Medical Genetics and Genomics (ACMG) recommends that laboratories return secondary findings to individuals undergoing whole exome sequencing. The ACMG selects genes to include that are associated with conditions that have the potential to be treated or avoided. Examples of these conditions include some hereditary cancer and cardiac conditions. Please refer to the latest version of the ACMG Recommendations for Reporting of Secondary Findings in Clinical Exome and

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Genome Sequencing for complete details of the genes and associated genetic disorders that are included as secondary findings.

Individuals undergoing whole exome sequencing can decide whetheror not they would like to receive these results. Individuals can choose to opt in to receiving secondary findings by marking the checkbox on the Proband Consent signature page or the Family Member Consent signature page. If nothing is checked, they will be opted out. If parental samples are included for testing and they elect to receive secondary findings they will receive an individual report with their secondary findings results.

The following are the possible types of results I, or my child, may receive if we elect to receive secondary findings:

1. **Positive:** A positive secondary findings result means that a genetic variant or multiple genetic variants were identified in one or more of the ACMG recommended genes. Individuals with positive secondary findings results may need to undergo additional screening or clinical management. In addition, a positive secondary finding result may mean that additional family members are at risk and should be offered genetic counseling/genetic testing.
2. **Negative:** A negative secondary findings result means that no reportable variant was identified within the ACMG recommended genes. A negative secondary findings result does not eliminate the possibility that I, or my child, has one of the genetic conditions that was included on the test. If an individual has a personal or family history of one of the conditions tested as part of the secondary findings, it is recommended that they discuss this with their doctor or a genetic counselor, as this testing is not a substitute for comprehensive genetic testing for these conditions.

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Proband Consent

I have read the Informed Consent document and I give permission to Genosity to perform genetic testing as described. My signature below acknowledges that my, or my child's, healthcare provider has ordered genetic testing. I understand the potential outcomes, including the benefits, risks and limitations of this testing as described above. I have had the opportunity to ask questions prior to giving my informed consent and my questions have been satisfactorily answered. I also acknowledge that it is my responsibility to contact my healthcare provider to discuss the reported result.

___Check this box if you wish to receive secondary findings

___ Check this box if you do NOT wish to have your sample stored beyond 60 days after the completion of testing.

For NY State Residents only:

__ Check this box if you wish to have your sample stored for research and quality control purposes. If this box is not checked, the sample, and all materials derived from it (i.e. DNA) will be destroyed within 60 days of test completion

_____

Patient Signature | Patient Name | Date (MM/DD/YYYY)

_____

Parent/Guardian Signature *(if patient is a minor/disabled)* | Parent/Guardian Name | Date (MM/DD/YYYY)

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Family Member Consent

As a family member involved in this test, I have read the Informed Consent document and I give permission to Genosity to perform genetic testing as described. My Signature below acknowledges that my healthcare provider has ordered genetic testing. I understand the potential outcomes, including the benefits, risks and limitations of this testing as described above. I have had the opportunity to ask questions prior to giving my informed consent, and my questions have been satisfactorily answered. I acknowledge that it is my responsibility to contact my healthcare provider to discuss the reported result.

___Check this box if you wish to receive secondary findings

___ Check this box if you do NOT wish to have your sample stored beyond 60 days after the completion of testing.

For NY State Residents only:

__ Check this box if you wish to have your sample stored for research and quality control purposes. If this box is not checked, the sample, and all materials derived from it (i.e. DNA) will be destroyed within 60 days of test completion.

_____

Signature Printed Name Relationship to The Patient Date (MM/DD/YYYY)

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