FullGenomics

HERES Carrier Screening test
Information for Clinicians

FullGenomics introduces to you HERES, a carrier screening test that enables us to provide you and your patients with valuable information essential in pregnancy and family planning.

What is carrier screening?

Carrier screening uses genetic testing to identify carrier couples and individuals at risk for passing genetic disorders on to their children. These genetic disorders can include physical disabilities, cognitive impairment, and other severe health problems.

Generally, everyone inherits two copies of each gene: one from their mother and one from their father. A carrier is an individual who has one mutated copy and one normal copy of the same gene. Carriers typically do not have signs or symptoms of a genetic disorder.

Traditionally, carrier screening has targeted couples of certain ethnic groups with a high risk of carrying specific genetic disorders. This approach presented difficulties for patients who are multiracial, adopted, or unsure of their ethnic backgrounds. To address this concern, expanded carrier screening (ECS) was developed to look for mutations that cause a wide variety of genetic disorders regardless of a patient's ethnicity.

The American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics and Genomics (ACMG) have published guidelines on expanded carrier screening and its importance in reproductive care.

How are genetic disorders inherited?

HERES Carrier Screening scans genes for mutations that cause autosomal recessive and X-linked recessive disorders.

An **autosomal recessive disorder (AR)** occurs when a child inherits two mutated copies of a gene - one from each carrier parent. If both partners are carriers of the same AR disorder, there is a 1 in 4 (25%) chance their baby will be affected with that disorder.

X-linked recessive (XLR) conditions occur due to a mutated gene located on the X chromosome. Because males only have one X chromosome, a male will be affected if he inherits a mutated gene from his mother. Because females have two X chromosomes, carrier mothers and daughters usually do not display symptoms. For XLR conditions, only the mother has to be a carrier for her children to be at risk. If she is a carrier, there is a 1 in 2 (50%) chance her son will be affected.

Why should I offer carrier screening to my patients?

Genetic disease accounts for ~20% of infant mortality and ~18% of pediatric hospitalizations in the United States. Many children born with a genetic disorder have parents who are carriers of the disorder. Research has shown that most people are a carrier for at least one genetic disorder; however, many are not aware of their carrier status until after the birth of a child with the disease.

To assist couples in discovering their carrier status, screening should be offered before or during pregnancy to women of reproductive age and their reproductive partners, as well as to gamete (egg or sperm) donors. Carrier screening will assist in preconception planning and prenatal diagnostic testing for couples identified as carriers.

If both partners are found to be carriers for the same recessive disorder, then prenatal testing such as chorionic villi sampling (CVS) or amniocentesis could determine if the baby is affected with the recessive disorder. Additionally, in vitro fertilization (IVF) with preimplantation genetic diagnosis (PGD) may be considered to reduce the risk of having an affected child.

Why choose HERES Carrier Screening?

HERES Carrier Screening:

- Analyzes 301 genes, in which mutations may cause 313 different recessive disorders.
- Provides full coverage of each gene via CNVexon™, a specialized method to detect different types of mutations by using one technology.

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HERES Carrier Screening Panels:

HERES SEQ: a pan-ethnic test that screens for the most common genetic disorders seen within the general population. Carrier screening for these disorders has been recommended by the American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics and Genomics (ACMG).

HERES GEN: is the pan-ethnic carrier screening panel used to identify carriers of specific pathogenic variations of more than 300 autosomal recessive and X-linked disorders within the general population.

Note: *Male patients will not be screened for X-linked conditions. If an X-linked condition is suspected in a male patient, please contact FullGenomics or a genetics professional about diagnostic testing for that specific disorder.*

Testing Methodologies

HERES Carrier Screening performs the deepest search possible for pathogenic carrier variations by combining different genetic technologies and applying cutting-edge bioinformatics to detect these variations in over 300 genes.

Next Generation Sequencing and Deletion/Duplication Analysis

HERES is the only carrier screening that offers sequencing and deletion/duplication analysis for over 300 genes. Sequencing reads the DNA code of a gene or several genes, one base at a time, to determine an individual's sequence. The sequence is then compared to a reference DNA sample to detect any variants found within the patient's DNA. Next generation sequencing (NGS) is used to analyze exons in multiple genes simultaneously. We use a sophisticated method, CNVexon™, that detects sequence changes and deletions/duplications (del/dups) via NGS. The ability to detect sequence variants and del/dups through CNVexon™ allows HERES to offer the best coverage through a cost-effective and highly accurate technology.

Note: *Sometimes genetic material that resembles a real gene (pseudogene) or genes that contain similar sequences may interfere with the ability to identify mutations via NGS. To bypass this issue, we use highly sensitive tools that are capable of identifying carrier variations in disease genes (such as GBA for Gaucher disease and HBA1/HBA2 for alpha-thalassemia) without the risk of pseudogene interference.*

PCR

PCR amplification is used to detect the CGG repeat expansion of the FMR1 gene. When the CGG repeat expands to a specific number, it can cause fragile X syndrome. We can also detect AGG interruptions, which may decrease the risk of the CGG repeat expansion when inherited from the mother.

Testing Limitations

All laboratory tests have limitations. A positive result does not imply that there are no other mutations in the patient's genome, and negative results do not eliminate the risk for the patient's children to be affected with a genetic disorder. HERES Carrier Screening is not designed to detect somatic mutations. Mutations that are not located in the exons of genes may not be detected by this test.

Detection Rates

A broad range of laboratory and bioinformatic tools are employed to ensure the highest detection rate of any carrier screening panels on the market. HERES's analytical detection rate for all genes is >98%. The clinical detection rate varies by disease. Residual risk is the chance that the patient being screened is a carrier even after a negative screening test result.

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Specimen and Shipping Requirements

FullGenomics accepts blood and saliva samples for HERES Carrier Screening panels.
Please see below for shipping requirements:

Blood

•Two 4-mL EDTA (lavender top) tube.
•This is our preferred specimen type for testing. Blood specimens can be sent at ambient temperature if express delivery is arranged such that arrival is within 72 hours of collection. Otherwise, samples will need to be refrigerated.

Saliva / Buccal Swab

•Saliva / buccal swab specimens can be sent at ambient temperature if express delivery is arranged such that arrival is within 72-96 hours of collection.
•For del/dup analysis, blood samples are preferred as buccal swabs may fail to generate high quality data.

Turnaround Time

Once the sample is received at the lab, results will be available in approximately three weeks.

Reports

Only variants classified as “Pathogenic” or “Likely Pathogenic” using the ACMG standards and guidelines for the interpretation of sequence variants will be reported.

FullGenomics’s Genetic Counseling Service

Once the carrier screening test is completed, FullGenomics offers genetic counseling to patients who have questions about their results. Our genetic counselors are also available to answer questions healthcare providers may have about testing.

References

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3. Edwards et al. Expanded Carrier Screening in Reproductive Medicine--Points to Consider. A Joint Statement of the American College of Medical Genetics and Genomics, American College of Obstetricians and Gynecologists, National Society of Genetic Counselors, Perinatal Quality Foundation, and Society for Maternal-Fetal Medicine. Obstet Gynecol 2015; 1253.
4. Gross SJ et al. Carrier screening in individuals of Ashkenazi Jewish descent. ACMG Practice Guidelines. Genet Med 2008:10(1):64-56.
5. Kingsmore S. Comprehensive Carrier Screening and Molecular Diagnostic Testing for Recessive Childhood Diseases. PLoS Currents. 2012;4:e4f9877ab8ffa9. doi:10.1371/4f9877ab8ffa9.