Beacon Expanded Carrier Screening

Fulgent Genetics has developed Beacon, the most comprehensive and accurate expanded carrier screen enabling us to provide you and your patients with valuable information essential in pregnancy and family planning.

What is carrier screening?

Carrier screening is a genetic test used to identify carrier couples and individuals at risk for passing genetic disorders to their children. These genetic disorders may cause babies to have physical disability, cognitive impairment, and other severe health problems.

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

Professional medical associations, 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.

What is a carrier?

Before we continue, let's review some basic genetics.

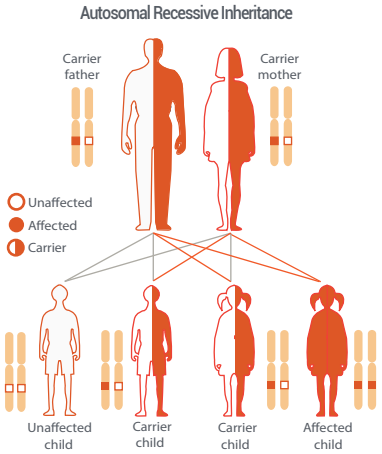
Genes are pieces of DNA that instruct our bodies on how to grow and develop. We all have millions of genetic changes; many are benign and do not cause disease or impact our health. However, some changes in genes may be harmful and may cause disease in an individual or when passed down to his or her children. These harmful changes are called mutations or "pathogenic variants" and prevent the gene from working properly, ultimately causing a genetic disorder. Most carrier screens scan genes for mutations that cause autosomal recessive and X-linked recessive disorders.

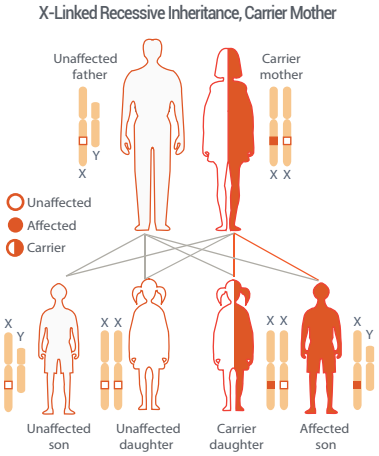
For most genes, everyone inherits two copies: one from mom and one from dad. A carrier is an individual who has one mutated copy and one normal copy of the same gene. Carriers typically do not have signs or symptoms of a genetic disorder.

How are genetic disorders inherited?

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?

Collectively, genetic disease accounts for ~20% of infant mortality and ~18% of pediatric hospitalizations in the United States. Many babies 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. A carrier will only know his or her status after screening or after the birth of a child with the disease.

To assist couples in discovering their carrier statuses, screening should be offered during or before pregnancy to women of reproductive age, their reproductive partners, and to gamete (egg or sperm) donors. Carrier screening is important and 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 or not to help manage a current or future pregnancy. Additionally, in vitro fertilization (IVF) with preimplantation genetic diagnosis (PGD) may be considered to reduce the risk of having an affected child.

Why choose Beacon Carrier Screening?

Beacon carrier screening:

- Analyzes more than 300 genes, in which mutations may cause over 330 different recessive disorders,
- Provides full coverage of each gene via CNVexon™, a specialized method to detect different types of mutations by using one technology, providing highly accurate results while remaining cost-effective, and
- Can be customized: Fulgent Genetics understands not every couple has the same needs and each patient's circumstances will differ, therefore we have designed 5 different carrier screening panels. As the ordering physician, you can add or remove any genes within the full set or create the most suitable panel for your patients with a **Beacon Custom panel**. Click [insert link to main BECS test menu] to explore all Beacon Carrier Screening options.

Beacon Carrier Screening Panels:

Beacon ACOG/ACMG panel screens for the most common genetic disorders seen within the general population. Carrier screening for these disorders have been recommended by the American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics and Genomics (ACMG).[2,6]

Beacon Ashkenazi Jewish panel analyzes genes for pathogenic carrier mutations known to cause recessive disorders seen at high carrier frequencies within the Ashkenazi Jewish population. In addition to spinal muscular atrophy (SMA) and fragile X syndrome, ACOG recommends that couples of Ashkenazi Jewish ancestry be offered carrier screening for Tay-Sachs disease, Canavan disease, cystic fibrosis, and familial dysautonomia. Furthermore, advocacy groups, such as the Jewish Genetic Disease Consortium, also recommend testing for other disorders such as mucolipidosis IV, Niemann-Pick disease type A, Fanconi anemia group C, Bloom syndrome, and Gaucher disease.[2,4] Visit the Jewish Genetic Disease Consortium website to view the full list of genetic disorders recommended for carrier screening for Jewish couples.

Beacon Focus panel is the pan-ethnic carrier screening panel used to identify carriers of 30 autosomal recessive and X-linked disorders with high carrier frequencies within the general population and within a few specific populations.

Beacon Expanded panel screens for more than 300 conditions not specific to any one population although, some diseases are more common than others or more common to a specific ethnic group. These conditions vary in morbidity, mortality and treatment.

Beacon Expanded + Opt-In panel is the largest carrier screening panel available. All genes from the Beacon Expanded Carrier Screening panel are included with the addition of 9 "opt-in" genes that are associated with mild or adult-onset presentation of disease, but may be of interest to specific families or clinics.

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

Testing Methodologies

Beacon Carrier Screening does the deepest search possible for pathogenic carrier mutations by combining different genetic technologies and applying cutting-edge bioinformatics to detect these mutations in over 330 genes.

Next Generation Sequencing and Deletion/Duplication Analysis

Beacon is the only carrier screening that offers sequencing and deletion/duplication analysis for over 330 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 changes found within the patient's DNA. Next generation sequencing (NGS) is used to analyze exons in multiple genes simultaneously. Fulgent Genetics has developed a sophisticated method, CNVexon™, that detects sequence changes and deletions/duplications (del/dups) via NGS. Having the ability to detect sequence variants and del/dups through CNVexon™, Beacon offers the best coverage through a cost-effective and highly accurate technology.

*Pseudogenes

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, Fulgent Genetics has developed highly sensitive tools that are capable of identifying carrier mutations in disease genes (such as GBA for Gaucher disease and HBA1/HBA2 for alpha-thalassemia) that apply to this description.

PCR

PCR amplification is used to detect the CGG repeat expansion of the FMR1 gene. When the CGG repeat expands to a specific number of repeats, 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 to child.

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. Beacon carrier screening is not designed to detect somatic mutations. Mutations that not are 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 out of any carrier screening panels on the market. Beacon's analytical detection rate for all genes is >98%. The clinical detection rate varies by disease (see Supplemental Table online). Residual risk is the chance the patient being screened is a carrier after a negative screening test result. Fulgent uses an in-house algorithm to calculate residual risk for carrier couples.

Specimen and Shipping Requirements

Fulgent accepts blood and saliva samples for Beacon carrier screening panels. Visit www.FulgentGenetics.com to order the appropriate test kit. Please see below for shipping requirements:

Blood

• Two 4ml in EDTA (lavender top) or ACD (yellow top) tubes, or one of each is required.

• This is our preferred specimen type to receive for testing. Blood specimens can be sent at ambient temperature and express delivery should be arranged such that it arrives within 72 hours from collection, otherwise, they will need to be refrigerated.

Saliva / Buccal Swab

• DNA Genotek OC-100 kits are preferred and can be provided upon request.

• Saliva / buccal swab specimens can be sent at ambient temperature and express delivery should be arranged such that it arrives within 72 to 96 hours from when it was sent.

• 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, the results will be available in approximately 2 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.

Fulgent's Genetic Counseling Service

Once the carrier screening test is completed, Fulgent Genetics 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. Patients can schedule Genetic Counseling Service online, visit www.FulgentGenetics.com for details.

Cost/Insurance

Fulgent accepts all commercial and private healthcare insurance plans. Our insurance specialists can verify insurance coverage either before or after a sample is received in the laboratory. Prior to testing, we will contact your patient if there is an anticipated out-of-pocket cost that exceeds $100. We also offer self-pay and institutional billing options, financial assistance, and no-interest payment plans to those who qualify. Please contact us for additional information about our billing options.

References

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4. Gross SJ et al. Carrier screening in individuals of Ashkenazi Jewish descent. ACMG Practice Guidelines. Genet Med 2008:10(1):64-56.

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