ACOG/ACMG Carrier Screen: Gene Sequencing Panel

Test Code: MM570  
Turnaround time: 4 weeks  
CPT Codes: 81223 x1, 81405 x1, 81406 x1

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<th>Condition Description</th>
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Test components:

- Carrier screening for cystic fibrosis as recommended by the American College of Medical Genetics (ACMG) and the American Congress of Obstetricians and Gynecologists (ACOG)
- Carrier screening for four conditions (Tay-Sachs, Canavan disease, cystic fibrosis, and familial dysautonomia) common to those of Ashkenazi Jewish descent, as recommended by ACOG, and five additional conditions (Bloom syndrome, Fanconi anemia type C, Gaucher disease, Niemann-Pick type A, and Mucolipidosis IV), as recommended by ACMG
- Carrier screening for spinal muscular atrophy (SMA) as recommended by ACMG

Click here for a complete list of conditions.

With the utilization of next generation sequencing, carrier screening panels have been expanding to cover more and more conditions over the last five years. Although 47% of physicians note patients requesting this expanded testing, 37% of physicians prefer to only offer testing recommended by the professional societies. To address this need, the ACOG/ACMG Carrier Screen was developed. This screen only incorporates conditions specifically recommended by at least one of these societies.

This panel is available as full gene sequencing or targeted mutation analysis. EGL also offers single-gene sequencing for all genes on the panel, which may be utilized to more completely screen partners of positive carriers.

Although a positive test result should not affect the health of the individual, she could be at a 25% risk for passing that condition on to her children depending on the carrier status of the partner. In addition to the specific pathogenic variants identified by the panel, Emory Genetics Laboratory also offers single-gene, full gene sequencing for genes on the panel, which can be utilized to screen partners of positive carriers. Knowing about these risks ahead of time can help couples make decisions about testing options prior to and during pregnancy, and can help healthcare providers be more readily prepared to offer appropriate follow-up care at delivery.

Please note that ACMG is not opposed to expanded carrier screening as long as the clinical implications of the condition and mutations are known, adult-onset and mild or incompletely penetrant diseases are limited, meaningful risks can be calculated, and proper consent is available.

References:


Genes:

- ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, SMN1, SMPD1

Indications:

This test is indicated for:

- Individuals or couples seeking to assess reproductive risk for a variety of conditions.
- Individuals or couples of high-risk ethnic groups or backgrounds.

Methodology:

Next Generation Sequencing: In-solution hybridization of all coding exons is performed on the patient’s genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Only known pathogenic variants will be reported.

Spinal Muscular Atrophy (SMA) Testing: SMN1 gene deletions were quantified by multiplex ligation polymerase chain reaction amplification (MLPA) of exons 7 and 8. Gene dosage ratios of SMN1 are calculated relative to the average of 16 reference loci and are expressed as gene dosage, and/or copy number. Diploid gene dose or 2 copies of SMN1 indicates normal (not affected) status, 1x gene dosage or 1 copy of the SMN1 gene most likely indicates carrier status and deletions (less than 0.1x) of SMN1 or 0 copies of the SMN1 gene designates affected status. This carrier assay tests for the common SMN1 deletion only; other pathogenic variants will not be detected. SMN2 copy number is not assessed.

Detection:

Next Generation Sequencing: Clinical Sensitivity: See results report. Pathogenic variants in regions other than the targeted area, including the promoter region, some mutations in the introns and other regulatory element mutations, cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's
clinical/biochemical phenotype.

**For Spinal Muscular Atrophy (SMA) Testing:** Deletions of the \( SMN1 \) gene are found in approximately 95% of individuals with SMA. This carrier assay tests for the common \( SMN1 \) deletion only; other pathogenic variants will not be detected. \( SMN2 \) copy number is not assessed.

### Reference Range

### Specimen Requirements

Submit only 1 of the following specimen types

**Type: Saliva**

Specimen Requirements:

- Oragene\textsuperscript{TM} Saliva Collection Kit.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Whole Blood**

Specimen Requirements:

- In EDTA (purple top) tube:
  - Infants (2 years): 3-5 ml
  - Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

- In microtainer: 60 \( \mu \)g

Isolation using the Qiagen\textsuperscript{TM} Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

### Related Tests

- ACOG/ACMG Carrier Screen: Targeted Mutation Panel
- Pan-Ethnic Carrier Screen: Gene Sequencing Panel
- Ashkenazi Jewish Carrier Screen: Gene Sequencing Panel