

## ACOG/ACMG Carrier Screen: Targeted Mutation Panel

**Test Code:** MM580

**Turnaround time:** 2 weeks

**CPT Codes:** 81220 x1, 81242 x1, 81251 x1, 81255 x1, 81260 x1, 81290 x1, 81330 x1, 81400 x1, 81200 x1, 81209 x1

### Condition Description

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 Mucopolidosis IV), as recommended by ACMG
- Carrier screening for spinal muscular atrophy (SMA) as recommended by ACMG

Click [here](#) for a complete list of mutations.

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.<sup>1</sup> 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, EGL Genetics 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.<sup>2</sup>

Condition	Gene	Mutations
Bloom Syndrome	<i>BLM</i>	2281del6ins7*, 2407insT, Q645X, Q700X, R899X
Canavan Disease	<i>ASPA</i>	433-2A>G, Y231X*, A305E, E285A*
Cystic Fibrosis	<i>CFTR</i>	142 mutation panel including 23 ACMG recommended mutations (see below)
Familial Dysautonomia	<i>IKBKAP</i>	2204+6T>C, R696P*
Fanconi Anemia Type C	<i>FANCC</i>	322delG, IVS4+4A>T*, R548X, Q13X, R185X, L554P
Gaucher Disease Type 1	<i>GBA</i>	84GG*, del55bp, IVS2+1G>A*, D409H, D409V, L444P*, N370S*, R463C, R463H, R496H, V394L
Mucopolidosis Type IV	<i>MCOLN1</i>	Exon1 - Exon7del (Del6.4kb)*, IVS3-2A>G*
Niemann-Pick Type A	<i>SMPD1</i>	fsP330*, R610del, H423Y, L302P*, R476W, R496L*, T324I
Spinal Muscular Atrophy	<i>SMN1</i>	Gene dosage
Tay-Sachs Disease	<i>HEXA</i>	1278insTATC*, del7.6kb, 1421+1G>C*, IVS7+1G>A, IVS9+1G>A, E462V, G250D, G269S*, R170W, R178H, R247W, R249W

\*Testing for these mutations is recommended by the American College of Medical Genetics (ACMG). *Genet Med* 2008;10(1):54-56.

Click [here](#) for a complete list of *CFTR* mutations.

References:

1. Benn P, Chapman AR, Erickson K, et al. Obstetricians and gynecologists' practice and opinions of expanded carrier testing and noninvasive prenatal testing. *Prenat Diagn.* 2014 Feb;34(2):145-52.
2. Grody WW, Thompson BH, Gregg AR, et al. ACMG position statement on prenatal/preconception expanded carrier screening. *Genet Med.* 2013 Jun;15(6):482-3.

### Genes

[ASPA](#), [BLM](#), [CFTR](#), [ELP1](#), [FANCC](#), [GBA](#), [HEXA](#), [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 the regions encompassing the targeted pathogenic variants is performed on the patient's genomic DNA. 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: DNA, Isolated

**Specimen Requirements:**

Microtainer

15µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

### Type: Whole Blood (EDTA)

**Specimen Requirements:**

EDTA (Purple Top)

Infants and Young Children ( 2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

## Related Tests

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