

Spinal Muscular Atrophy: Carrier Screen

Test Code: MM490

Turnaround time: 2 weeks

CPT Codes: 81401 x1

Condition Description

Spinal muscular atrophy (SMA) is the second most common lethal, autosomal recessive disorder in Caucasians, with an incidence of approximately 1/10,000 and a carrier frequency of 1/50. SMA is characterized by anterior horn cell degeneration which causes a symmetrical muscle weakness and wasting. Other symptoms can include joint contractures, respiratory insufficiency, and feeding and sleep difficulties. Subtypes have been created, although the phenotype can span a broad continuum and subtypes are not clearly delineated. Subtypes of SMA include:

- Type 0: prenatal onset of severe joint contractures and weakness at birth; lifespan ranges from days to 2-6 months
- Type I (Werdnig-Hoffman disease): most severe form of SMA with an onset of severe weakness before 6 months of age; affected individuals usually die by 2 years of age
- Type II (Dubowitz disease): intermediate in severity between Types I and III, with an onset of symptoms after 6 months of age; death occurs in childhood or young adulthood
- Type III (Kugelberg-Welander disease): mildest form of childhood onset SMA, with symptoms usually beginning after 10 months; affected individuals can survive into adulthood
- Type IV: onset of muscle weakness in second or third decade with normal lifespan

All SMA subtypes are caused by mutations in the survival motor neuron (*SMN1*) gene (5q11.2-q13.3). *SMN1* is deleted in about 95-98% of individuals with SMA. Point mutations are also known in this gene. Approximately 2-5% of affected individuals have one deletion and one point mutation. Approximately 2% of affected individuals have a de novo mutation meaning only one parent is an SMA carrier.

This carrier assay tests for the common *SMN1* deletion only; point mutations will not be detected. Approximately 5-8% of carrier individuals will have a normal *SMN1* copy number of two, but both copies will be on the same chromosome (in cis) with a deletion on the second chromosome. This assay will not detect these carrier individuals. This assay will not report *SMN2* copy number.

Visit www.ThinkGenetic.com for patient-friendly information on [spinal muscular atrophy](#).

Genes

[SMN1](#)

Indications

This test is indicated for:

- Carrier testing.
- Individuals or couples seeking to assess reproductive risk.

Methodology

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. The SMA component of this assay does not test for point mutations. *SMN2* copy number is not assessed.

Detection

Deletions of the *SMN1* gene are found in approximately 95% of SMA patients, but the frequency is less in the milder (type II and III) variants. Affected individuals with 0 copies of *SMN1* seem to have milder form of the disease with increased copy numbers of the *SMN2* gene. Deletions of the *SMN1* gene are the most common pathologic mechanism for SMA, however, other gene rearrangements have been described in affected individuals, including hybrid or fusion *SMN* genes and deleterious point mutations in the *SMN1* gene. Thus, the lack of a deletion does not necessarily rule out this diagnosis, and further testing may be required.

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:

Microtainer

3µg

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/ μ L 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

- Pan-Ethnic Carrier Screen
- Ashkenazi Jewish Carrier Screen
- Fragile X