Molecular Test for SMA (Spinal Muscular Atrophy)

The UNC Hospitals Molecular Genetics Laboratory offers diagnostic and carrier testing for Spinal Muscular Atrophy by molecular analysis of the *SMN1* & *SMN*2 genes. Spinal muscular atrophy is the most common lethal genetic disease in children, and is characterized by progressive muscle weakness due to degeneration of the lower motor neurons. Carrier screening of SMA will be used to guide genetic counseling, treatment and subsequent monitoring.

Biology of the Disease:

Spinal muscular atrophy (SMA) is an autosomal recessive disease characterized by degeneration of spinal cord motor neurons that leads to atrophy of skeletal muscle and overall weakness. The incidence of SMA is approximately 1 in 10,000 live births, and the disease is reported to be the leading genetic cause of infant death. For diagnosis of SMA, it is sufficient to detect the *SMN1* deletion. The severity and type of SMA correlates with the number of *SMN2* copies and with the presence or absence of the c.859G>C *SMN2* modifier variant. *SMN2* is highly homologous to *SMN1* but has several nucleotide changes that distinguish it from *SMN1* and also alter splicing so that it is not as efficient at making protein as *SMN1*. However, when *SMN1* is deleted, the more copies of *SMN2* an individual has, the less severe the SMA phenotype. Targeted treatments such as Spinraza® (which aim to upregulate protein production from any *SMN2* genes present) may prevent the development or slow the progression of some features of SMA. Efficacy is improved when treatment is initiated before symptom onset so timely testing and return of results is crucial. SMA carrier frequencies in most populations are estimated at 1 in 40 to 1 in 60. Silent carriers (individuals with two copies of *SMN1* on the same chromosome) can be inferred by testing two tightly linked *SMN1* variants: c.*3+80T>G and c.*211_*212del.

Clinical Indications for Testing: Diagnostic testing is performed to confirm a suspected diagnosis of SMA. Carrier testing is recommended by the American college of Obstetricians and Gynecologists (ACOG) for all individuals who are pregnant or considering pregnancy. Genetic counseling is recommended.

Laboratory testing for *SMN1/2*: The preferred sample is ACD or EDTA anticoagulated blood (pale yellow top or lavender top, 1- 3ml) which may be refrigerated up to 48 hours prior to testing.

The AmplideX® PCR/CE *SMN1/2* Plus assay is an *in vitro* PCR assay for determination of exon 7 copy number and the genotype status of relevant variants in the *SMN1* and *SMN2* genes, followed by capillary electrophoresis. The assay generates exon 7 copy numbers for both *SMN1* and *SMN2* reported as 0, 1, 2, 3, or ≥ 4 genomic copies, in addition to variant status for the gene duplication variants *SMN1* c.*3+80T>G and *SMN1* c.*211_*212del, as well as the disease modifier variant *SMN2* c.859G>C.

References:

1. Gene Reviews: https://www.ncbi.nlm.nih.gov/books/NBK1352/
2. The Muscular Dystrophy Association: https://www.mda.org/disease/spinal-muscular-atrophy

Questions?

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