Spinal Muscular Atrophy (SMA) Type I / II / III / IV – OMIM 253300 / 253550 / 253400 / 271150

Background

Spinal Muscular Atrophy (SMA) refers to a group of neuromuscular disorders that affect the nerves in an area of the spinal cord called the anterior horn. These nerve cells become damaged, and as a result, the muscles cannot be used and become wasted (atrophied). This inherited condition is caused by mutations in the *SMN1* gene (OMIM 600354) and has an autosomal recessive inheritance pattern; both parents usually carry the defective gene and pass it on for the child to be affected (in approximately 2% of cases one of the parents is not a carrier). There are several types of SMA, varying in severity, age of onset and which muscles are most affected – Types I, II and III start in infancy and are classed as severe, intermediate and mild respectively, and type IV is mild, adult onset.

Mutations causing SMA are generally deletions and gene conversion events of the *SMN1* gene, rare point mutations are also detected in a small number of cases. Variable copy number of the *SMN1* gene in the general population can have serious genetic counseling complications when determining carrier status. The closely related *SMN2* gene (OMIM 601627) also shows copy number variation, and can "rescue" the SMA phenotype to some extent.

Recommended Clinical Referral Criteria

- Autosomal recessive family history of the condition
    - Patients may be referred as either diagnostic cases or for determination of carrier status
- Clinical picture consistent with SMA

Molecular Analysis

Mutation screen: MLPA dosage analysis of *SMN1* gene to detect deletions and conversions; 95-98% cases are homozygous deleted*; 2-5% cases are compound heterozygotes for a deletion* / point mutation *For deletion = deletion or gene conversion
Family follow-up: Testing for known familial mutations in *SMN1* gene

Test (Price available on request)	**TAT (calendar days)**
Diagnostic dosage analysis (*SMN1/SMN2*)	42
Testing in neonates (*SMN1/SMN2)*	14
Family studies (*SMN1)*	42
Prenatal testing	3

Sample Requirements

Blood– 5ml in EDTA (1ml neonate/infant);
Please contact lab prior to sending a prenatal sample.
Please label samples with three identifiers and date of collection.
All samples must be accompanied by request form
Consent for testing & DNA storage is assumed when request is received

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Links

Orphanet
http://www.orpha.net/
OMIM
http://www.omim.org/
Genetic Test Registry
http://www.ncbi.nlm.nih.gov/gtr/

Support
Muscular Dystrophy Campaign
http://www.muscular-dystrophy.org/