*Bristol Genetics Laboratory is a UKAS accredited medical laboratory No.9307.*

North Bristol NHS Trust

# Spinal Muscular Atrophy (SMA)/ *SMN1* Gene

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**Sample Required**
**See Sample requirements page at www.nbt.nhs.uk/genetics for full details**

*Prenatal testing MUST be arranged with the laboratory well in advance.*

*Samples should be accompanied by a FULLY completed request form (available as download at www.nbt.nhs.uk/genetics or from the laboratory).*

*Please include details of test, family history, address including POSTCODE, NHS number, referring clinician and centre.*

**Consent and Storage:**
*All genetic testing requires consent.* **It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.**

*DNA is stored from* **ALL** *patients undergoing DNA testing, unless consent for this is specifically denied.*

*Stored material from all referrals may be retained for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.*

## Clinical Background and Genetics

- *SMA is an autosomal recessive inherited neuromuscular disorder with an incidence of approximately 1 in 10,000 and a carrier frequency of approximately 1 in 50.*
- *It is characterised by degeneration of the anterior horn cells of the spinal cord, leading to symmetrical muscle weakness and atrophy*
- *4 types – genetically similar but differ in patient age at presentation & clinical course:*
  1. **SMA type I** *(Werdnig-Hoffman) (OMIM: 253300): acute infantile SMA. Onset from birth to 6 months. Baby unable to rollover or sit – 'floppy baby'*
  2. **SMA type II** *(Dubowitz) OMIM: 253550): chronic infantile SMA. Presentation between 6-12 months. Able to sit unsupported but not able to stand unaided and unable to walk*
  3. **SMA type III** *(Kugelberg-Welander) (OMIM: 253400): Presentation after 18 months. Able to stand and walk but show proximal muscle weakness.*
  4. **SMA type IV** *(OMIM: 271150): adult-onset SMA*
- *SMA is caused by a deficiency of the Survival of Motor Neuron (SMN) protein, encoded by the SMN genes, located on 5q13.*
- *Approximately 95% of individuals with SMA have a homozygous deletion of exon 7 of SMN1, either as a result of homozygous deletion or a gene conversion event. Of the remaining cases, approximately 5% are compound heterozygous with a point mutation on one chromosome and a deletion/gene conversion*
- *The SMN1 gene is duplicated with a highly homologous copy called SMN2*
- *5% normal individuals are deleted for SMN2 and this is not thought to cause clinical symptoms of SMA but may modify the SMA phenotype*
- *Approximately 2% of SMA cases are due to de novo mutations*

## Service offered

*Multiplex Ligation-Dependent Probe Amplification (MLPA) is used to determine the copy number of exons 7 and 8 of the SMN1 gene on 5q13 MLPA* **does not detect point mutations** *within the SMN1 gene. If appropriate, point mutation testing is arranged via UKGTN*

## Referrals

- **Diagnostic testing:** *Molecular confirmation of a clinical diagnosis of the disease (referrals from Clinical Genetics, Paediatrics, Neurology)*
- **Carrier testing:** *for individuals with a family history of SMA (via Clinical Genetics)*
- **Prenatal testing***: where both parents are confirmed carriers, available by arrangement with Clinical Genetics*

## Clinical Advice*:*

*If clinical discussion is required we would recommend discussion with Clinical Genetics, St Michael's Hospital, Bristol (Tel: 0117 342 5652)*

## Target reporting Times

- *Diagnostic testing: 42 days*
- *Carrier testing: 42 days*
- *Urgent testing: 14 days*
- *Prenatal testing: 3 days*

## Quality

- *The laboratory takes part in the GENQA scheme for this service.*

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**DETAILS CORRECT AT DATE OF PRINTING ONLY.**
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