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 SWGLH Sample and Test Information tab at https://www.nbt.nhs.uk/south-west-genomic-laboratory-hub **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 https://www.nbt.nhs.uk/south-west-genomic-laboratory-hub 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 can be arranged with a specialist testing laboratory.

Referrals

- **Diagnostic testing (National Genomic Test Directory code: R70):** Molecular confirmation of a clinical diagnosis of the disease (referrals from Clinical Genetics, Paediatrics, Neurology)
- **Carrier testing (National Genomic Test Directory code: R244 / R252):** 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 5107)

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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