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

North Bristol NHS Trust

R72 Myotonic Dystrophy Type 1 – *DMPK* gene

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

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 and postcode, NHS number, referring clinician and unit/hospital.

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 unless consent for this is specifically denied.

Stored samples may be used for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

- Myotonic Dystrophy type 1 (DM1, OMIM 160900) is an autosomal dominant disorder characterized by myotonia, muscular dystrophy, cataracts, hypogonadism, frontal balding and ECG changes.
- DM1 is caused by a CTG repeat expansion in the 3' untranslated region of *DMPK* (OMIM 605377) on chromosome 19.
- The severity of the disease varies with the number of CTG repeats:

Number of repeats	Stability of repeat	Myotonic dystrophy (DM) phenotype
5–35 (normal range)	Stable	No DM
36–50	May be unstable	No DM
51–150	Unstable	No, minimal or classical DM
>150	Unstable	Classical, juvenile or congenital DM

Ref: Kamsteeg et al European Journal of Human Genetics (2012) 20, 1203–1208

- There is a large degree of phenotypic variability between individuals so phenotypic predictions in individual cases should be made with caution.
- The CTG repeat is unstable and may increase in size upon parental transmission, especially if transmitted through the maternal germ line.
- This anticipation effect explains the occurrence of the severe congenital form of DM1 almost exclusively in the offspring of affected women.
- The severe congenital form of DM1 manifesting with hypotonia, failure to thrive and severe respiratory distress (but usually no myotonia or cataracts) is clinically distinct from the adult-onset form presenting in middle age.
- Patients with a strong clinical suspicion of myotonic dystrophy, and no expansion at the *DMPK* may be tested for an expansion at the DM2 locus (OMIM 602668). DM2 is caused by a CCTG repeat expansion in the *CNBP* gene (previously known as *ZNF9)* on chromosome 3 (OMIM 116955).

Service offered

- **Direct amplification of the CTG repeat is and Triplet-primed PCR (TP-PCR) analysis:** In combination these tests allow all genotypes to be detected and reported.
- Southern Blotting for sizing of large expansions is available via a separate laboratory if considered appropriate. Referrals are accepted from Clinical Genetics only.

National Genomics Test Directory R72:Myotonic dystrophy type 1

Referrals

- **Diagnostic testing:** Molecular confirmation of a clinical diagnosis of the disease. Requests are accepted from Clinical Genetics, Consultant Paediatric Neurologists and Consultant Neurologists.
- **Predictive testing:** For individuals with a family history of myotonic dystrophy, who request carrier testing. Requests are only accepted from Clinical Genetics.
- **Prenatal diagnosis:** For the foetus of a parent with a confirmed molecular diagnosis of DM1. Involvement of Clinical Genetics is essential. Prenatal referrals must be arranged with the laboratory well in advance.

Clinical Advice

- If clinical discussion is required we would recommend contact with Dr Andrew Norman, Consultant Clinical Geneticist, St Michael's Hospital, Bristol (Tel: 0117 342 5231).

Target Reporting Time

Diagnostic testing	42 days
Predictive testing and neonatal testing	14 days
Prenatal testing	3 days

Quality

- Bristol Genetics Laboratory participates in the GenQA scheme.

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