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Service information: Myotonic Dystrophy Type 1 (DM1)

Gene/Locus: ***DMPK*** **(19q13.32)** **OMIM: #160900 (*605377 – *DMPK* gene)**

Referrals: Clinical Geneticists, Neurologists, Paediatric Neurologist, other Relevant Specialities
Testing: Diagnostic testing offered in clinically affected patients, presymptomatic testing in patients at risk of developing DM1 (presymptomatic referrals are accepted from Clinical Genetics only)
Target Reporting Times:

• Routine diagnostic testing	28 calendar days	
• Diagnostic testing in neonates	5 working days	
• Presymptomatic testing	14 calendar days	from Clinical Genetics only
• Urgent testing*	3 calendar days	Prenatal diagnosis/diagnostic testing in pregnant women

***Please contact the laboratory for urgent testing.**

Test Details:

- **PCR across the *DMPK* CTG repeat region** to detect small expansions of the *DMPK* CTG repeats
- **Triplet-Primed PCR (TP-PCR)** of the *DMPK* CTG repeat region (using two different sets of primers) to detect larger pathogenic expansions of the *DMPK* CTG repeat region. TP-PCR cannot size the expansion.
- PCR analysis of **microsatellite markers** *may* be required to confirm the results of prenatal diagnosis, this will require samples from both parents.
- If **Southern blotting** is required to size a *DMPK* CTG repeat expansion or to investigate unusual cases, DNA can be forwarded to another laboratory for analysis. If Southern blotting is required, please contact the laboratory for reporting times.

Service Details:

Over 98% of myotonic dystrophy cases have an expansion of the *DMPK* CTG repeat region. Diagnostic testing using PCR and TP-PCR is predicted to detect pathological expansions of the *DMPK* CTG repeat region with high sensitivity in myotonic dystrophy type 1 (DM1). The following allele size ranges are used:
Normal 5-35 repeats; Intermediate 36-50 repeats - possible expansion in future generations; Full mutation >51 repeats - clinical features of DM1 (based on Kamsteeg *et al.* 2012.EJHG. 20, 1203-1208).

Individuals affected with myotonic dystrophy but without a pathological expansion in the *DMPK* gene may be affected with myotonic dystrophy type 2 (DM2, OMIM #602668; also known as PROMM) (Liquori *et al.*, 2001, Science 293: 867-867). If a patient has symptoms consistent with DM2, e.g. mild phenotype or late onset of symptoms, DNA can be forwarded to another laboratory for DM2 testing (*CNBP* gene). However, the funding for this will need to be provided by your department. If you require this service then please contact the laboratory.

Sample Requirements:

- **EDTA** blood sample (1-4 ml), labelled with patient's **full name**, **date of birth** and **NHS number**, or genomic DNA (≥20 µl at ≥50 ng/µl for routine testing, 7-20 µg DNA if Southern blotting is required). Please send two separate blood samples for presymptomatic testing.
- Samples should be accompanied by a **fully** completed referral card which should include the patient's full name, date of birth and NHS number.
- Please also include details of the test, relevant clinical details and full details of the referring clinician/centre
- Parental samples are required in some cases of prenatal diagnosis (see above).

Consent:

Please note that in submitting a sample, it is the responsibility of the clinician to ensure that consent has been taken i) for testing, ii) for storage, and iii) for the use of this sample and the information generated to be shared with the patient's relatives and their health professionals. Following testing, a sample of the patient's DNA may also be used anonymously to validate new tests and for internal quality control purposes.