AWMGS
All Wales Medical Genomics Service

Muscular Dystrophies: Myotonic Dystrophy (DM1) – OMIM 160900; Proximal Myotonic Myopathy (PROMM / DM2) – OMIM 602668

Background

Muscular dystrophy describes a large number of inherited conditions where muscles weaken. These diseases are progressive and different muscle groups are affected depending upon the type of muscular dystrophy, usually leading to some sort of disability. Myotonic Dystrophy (DM) tends to affect the face, jaw and neck rather than the larger weight-bearing muscles, and heart problems can be experienced; progression is commonly slow. DM types 1 and 2 are caused by defects in the genes *DMPK* (OMIM 605377) and *CNBP* (OMIM 116955) respectively; both have a dominant inheritance pattern - a 50% chance of an affected adult passing the condition onto their child. Type 1 may be categorized into mild, classic or congenital phenotypes. Mild DM1 is characterized by cataract and mild myotonia, with a normal life span. Classic DM1 is characterized by muscle weakness and wasting, myotonia, cataract, and often cardiac conduction abnormalities; adults may have a shortened life span. Congenital DM1 is characterized by hypotonia and severe generalized weakness at birth, often with respiratory insufficiency and early death. Type 2 is characterized by myotonia and muscle dysfunction with onset generally in the third decade. Both disorders show anticipation, decreasing age of onset and increasing severity with inheritance through a multi-generational family.

Recommended Clinical Referral Criteria

- Diagnostic cases and at-risk family members
- Autosomal dominant inheritance
- Adult onset (DM1 and DM2)
  - Muscle weakness and wasting, myotonia, cataracts and often cardiac conduction abnormalities
- Congenital onset (DM1 only)
  - Hypotonia and severe generalised weakness at birth, often with respiratory insufficiency and early death

Molecular Analysis

DM1: Fragment length analysis of *DMPK* gene [CTG]n triplet repeat expansion by PCR and triplet primed PCR
DM2: Fragment length analysis of *CNBP* gene [CCTG]n quadruplet repeat expansion by PCR and triplet primed PCR

Test (Price available on request)	**TAT**
DMPK expansion analysis	42cd
CNBP expansion analysis	42cd
Predictive analysis for either *DMPK* or *CNBP*	28cd

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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

Links

Orphanet
http://www.orpha.net/
OMIM
http://www.omim.org/
National Genomic Test Directory
https://www.england.nhs.uk/wp-content/uploads/2018/08/rare-and-inherited-disease-eligibility-criteria-v4.pdf
Support
Muscular Dystrophy Campaign
www.muscular-dystrophy.org