

Molecular Genetics Service Profile

Autosomal dominant Multiple Epiphyseal Dysplasia (MED)

Introduction

- ◇ MED (MIM 600969) is an osteochondrodysplasia affecting at least 1 in 10,000 individuals and is characterised by mild to moderate short stature and pain and stiffness in the joints. Radiographic features include delayed and irregular ossification of numerous epiphyses.
- ◇ Autosomal dominant MED shows considerable genetic heterogeneity - approximately 25-30% cases are due to mutations in the cartilage oligomatrix protein gene (*COMP*), approximately 10% cases are due to mutations in the genes encoding the $\alpha 1$, $\alpha 2$, $\alpha 3$ chains of Type IX collagen (*COL9A1*, *COL9A2*, *COL9A3*) and approximately 5% cases are due to mutations in the Matrilin-3 gene (*MATN-3*) (Briggs & Chapman, 2002).
- ◇ A recessive form of MED is also recognised, which is due to mutations in *DTDST* (see recessive MED service profile).

Contact details for the laboratory carrying out the genetic test for AD MED
c/o National Genetics Reference Laboratory (Manchester), Regional Genetics Services, St. Mary's Hospital, Hathersage Road, Manchester, M13 0JH UK
Dr. Jacky Taylor. Tel: +44 (0) 161 276 3202. Fax: +44 (0) 161 276 4058. Email: jacky.taylor@cmmc.nhs.uk

Reasons for referral

- ◇ Mutation screening in patients with clinically confirmed, or a differential diagnosis of MED.
- ◇ Presymptomatic testing of relatives of an index case with a previously identified mutation.
- ◇ Prenatal diagnosis may be relevant, and can be offered by our laboratory on prior arrangement. However, we strongly recommend that this should only be offered within the context of genetic counselling. In addition, the mutation in the parent must be known.
- ◇ Screening for unknown mutations is labour intensive, therefore we cannot accept urgent referrals of this type.

Samples

- ◇ Minimum 100 μ g of DNA from peripheral lymphocytes from your local laboratory. Blood samples (minimum of 5mls in EDTA) can also be sent to our laboratory by express mail (FedEx / UPS). Prenatal samples must be sent with a maternal sample. Please contact our laboratory (as above) for further details.

Technical

- ◇ Mutation scanning of exons 8-19 of *COMP* by fluorescent bi-directional sequencing.
- ◇ Mutation scanning of exon 8 of *COL9A1*, exon 3 of *COL9A2*, exon 3 of *COL9A3* is by fluorescent bi-directional sequencing.
- ◇ Mutation scanning of exon 2 of *MATN-3* is by fluorescent bi-directional sequencing.

Target turn-round time

- ◇ Mutation scanning of *COMP* exons 8-19, *COL9A1*, *COL9A2*, *COL9A3* and *MATN-3* by sequencing – 30 weeks. Routine, single mutation test - 4 weeks. Urgent, single known mutation test - 2 weeks. Pre-natal diagnosis – 2 weeks, however, this should be discussed with our laboratory (see above for contact details) prior to submission of samples.
- ◇ Turn-round times are from the receipt of all required samples and information, including appropriate clinical information and radiographs. Relevant clinical-radiographic expertise is currently offered at no cost through the use of the secure online submission system (the **ESDN Case Manager**). Testing is only performed after clinical and radiographic evidence has been reviewed using the **ESDN Case Manager**. To obtain a username and password for the **ESDN Case Manager** please email info@esdn.org.

Cost

- ◇ Level 1 MED mutation screen (*COMP* exons 10 – 15, *MATN-3* exon 2) cost €821. Level 2 MED mutation screen (including *COMP* exons 8 + 9, and 16 – 19) additional cost: €657. Level 3 MED mutation screen (including *COL9A* exons as above) additional cost €493.

References

- ◇ Briggs & Chapman. (2002). *Hum. Mut.* **19**: 465-478.

ESDN Project Administrator contact details

- ◇ Dr. Jacky Taylor. Tel: +44 (0) 161 276 3202. Fax: +44 (0) 161 276 4058. Email: jacky.taylor@cmmc.nhs.uk

Please photocopy and distribute this sheet as required

-An integrated Research and Diagnostic Network of Eight European Centres of Excellence-

