

## 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.
- ◇ Although autosomal dominant MED shows considerable genetic heterogeneity mutations are identified in approximately 75% of MED cases screened for the following genes; cartilage oligomatrix protein gene (*COMP*), the matrilin-3 gene (*MATN-3*) and the genes encoding the  $\alpha 1$ ,  $\alpha 2$ ,  $\alpha 3$  chains of Type IX collagen (*COL9A1*, *COL9A2*, *COL9A3*) (Kennedy *et al* 2005; Zankl *et al* 2007).
- ◇ A recessive form of MED is also recognised that is due to mutations in the DTDST gene (*SLC26A2*: see recessive MED service profile).

Contact details for the laboratory carrying out the genetic test for AD MED  
c/o Regional Molecular Genetics Service, Department of Medical Genetics, DNA Lab, First Floor,  
St. Mary's Hospital, Hathersage Road, Manchester, M13 0JH UK  
Dr. Gail Jackson. Tel: +44 (0)161 276 6122. Fax: +44 (0) 161 276 6606. Email: [Gail.Jackson@cmft.nhs.uk](mailto:Gail.Jackson@cmft.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 $\mu$ 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 exons 1-7 of *COMP* may also be undertaken if thought necessary).
- ◇ Mutation scanning of exon 2 of *MATN-3* is by fluorescent bi-directional sequencing (mutation scanning of the remaining exons of *MATN3* may be undertaken if thought necessary).
- ◇ Mutation scanning of exon 8 of *COL9A1*, exon 3 of *COL9A2* & exon 3 of *COL9A3* (including the splice donor and acceptor sites) by fluorescent bi-directional sequencing.

#### Target turn-round time

- ◇ Mutation scanning of *COMP* exons 8-19, *MATN-3*, *COL9A1*, *COL9A2* & *COL9A3* by sequencing– 8 weeks. Routine, single mutation test - 2 weeks. Pre-natal diagnosis – 3 days, 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](mailto:info@esdn.org).

#### Cost

- ◇ Full MED mutation cost €544. This service is currently covered by ESDN only when referrals are made through the **ESDN Case Manager**.

#### References

- ◇ Briggs & Chapman. (2002). *Hum. Mut.* **19**: 465-478; Kennedy *et al* (2005). *Eur J Hum Genet.* **13(5)**: 547-555; Zankl *et al* (2007) *Eur J Hum Genet.* **15(2)**:150-4.

#### ESDN Administrator contact details

- ◇ Email: [info@esdn.org](mailto:info@esdn.org) Website: [www.esdn.org](http://www.esdn.org)

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