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 with mutations identified in approximately 75% of cases screened for the following genes; cartilage oligomatrix protein gene (*COMP*), the matrilin-3 gene (*MATN3*) and the genes encoding the α1, α2, α3 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, Genetic Medicine, 6th Floor,
St. Mary's Hospital, Oxford Road, Manchester, M13 9WL UK
Dr. Gail Jackson. Tel: +44 (0)161 276 6645. Fax: +44 (0) 161 276 6606. Email: 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 100μg of DNA from peripheral lymphocytes from your local laboratory or a blood sample in EDTA (minimum of 10mls in adults/ 5mls in children) can be sent by first class post within the UK, or express mail out with the UK (FedEx/UPS). Prenatal samples must be sent with a maternal sample and advance notice is mandatory.

Technical

- Mutation analysis by PCR and bi-directional fluorescent sequencing of exons 8-19 of *COMP*, exon 2 of *MATN3* , exon 8 of *COL9A1*, exon 3 of *COL9A2 &* exon 3 of *COL9A3* (including the splice donor and acceptor sites). This should detect approximately 75% of MED mutations.

Target turn-round time

- Full mutation scanning: 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 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 (**also see**: http://www.mangen.org.uk/professionals/service-results/service-details/AD-Multiple+Epiphyseal+Dysplasia.aspx)

- Full mutation screen: £483.
- Single mutation test: £138.
- Prenatal diagnosis: £276. **ADVANCE NOTICE IS MANDATORY**

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 Website: www.esdn.org

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