Molecular Genetics Service Profile
Thanatophoric dysplasia (TD)

Introduction

◊ TD (MIM 187600, 187610) is a lethal autosomal dominant disease affecting 1 in 50,000 newborns. Extremely severe dwarfism with macrocephaly, narrow thorax, facial dysmorphy and cloverleaf skull in some cases are clinical characteristics. Radiographic features include shortening of long bones with bowed (TD type I) or straight (TD type II) femurs, short ribs, marked platyspondyly with U–shape aspect of vertebrae.

◊ TD is caused almost exclusively by recurrent mutations in different domains of the Fibroblast Growth Factor Receptor 3 (FGFR3), (Tavormina *et al*. 1995; Rousseau *et al*. 1995, 1996).

Contact details for the laboratory carrying out the genetic test for TD
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Reasons for referral

◊ Mutation screening in foetuses or newborns with radiographically or echographically diagnosed TD (type I or II) or short-limb dwarfism evocative of TD.

◊ Prenatal diagnosis is **not** offered for TD.

Samples

◊ Minimum 5 μg of DNA from peripheral blood from your local laboratory. Blood samples (minimum of 5mls in EDTA), amniotic fluid (2-5 mls) or a skin biopsy can also be sent to our laboratory by express mail (Fed Ex or UPS). Please contact our laboratory (as above) for further details.

Technical

◊ Mutation analysis by direct bi-directional sequencing of exons 8, 10, 15 and 19 of *FGFR3*.

Target turn-round time

◊ Routine analysis to confirm clinical and radiological diagnosis (15 days). Screening for unknown mutations in other exons is labour intensive and will be performed only if solid clinical and radiological diagnosis of TD has been established. This may take several weeks (15-20 weeks) and may fail to reveal a *FGFR3* mutation. 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

◊ €200 for common mutations.

References

◊ Rousseau *et al*. (1995). *Nat Genet* **10**: 11-12.

◊ Rousseau *et al*. (1996). *Hum Mol Genet* **5**: 509-512.

◊ Tavormina *et al.* (1995). *Nat Genet* **9**: 321-328.

ESDN Administrator contact details

◊ Email: info@esdn.org Website: www.esdn.org

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