

## Molecular Genetics Service Profile

### Autosomal Recessive Multiple Epiphyseal Dysplasia (rMED)

#### Introduction

- ◇ rMED (OMIM No. 226900) is the mildest condition within the DTD dysplasia spectrum. Only a minority of patients have abnormal findings at birth, clubfoot being the commonest. The disorder is characterized by joint pain (usually in the hips or knees); mild brachydactyly; mild clubfoot deformity. Onset of pain is variable, usually in late childhood. Stature is usually within the normal range prior to puberty; in adulthood, stature is only slightly diminished, with the median height shifting from the 50th to the 10th percentile. Radiographic findings include flat epiphyses (femoral head, proximal humerus) with early arthritis; mild brachydactyly; and double layered patella seen on lateral knee x-rays.
- ◇ rMED is caused by mutations in the *DTDST* (*SLC26A2*) gene coding for a sulphate transporter. Most patients are homozygous for R279W mutation, but other mutations (e.g., C653S and IVS1+2T>C) may be seen associated with rMED phenotype.

#### Contact details for the laboratory carrying out the genetic test for rMED

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#### Reasons for referral

- ◇ Mutation analysis in patients with a diagnostic suspicion of rMED on clinical and radiographic grounds; differential diagnosis of epiphyseal dysplasias.
- ◇ Carrier testing of relatives of an index case with a previously identified mutation.
- ◇ Prenatal diagnosis may be an option. We recommend that this be offered only within the context of appropriate genetic counselling. Moreover, prenatal testing is possible only in families where the mutations in the index case have been confirmed in advance. Screening for unknown mutations in a prenatal sample is not feasible.

#### Samples

- ◇ Screening for frequent mild mutations associated with the rMED phenotype: minimum 10µg of DNA extracted from peripheral lymphocytes or fibroblasts from your local laboratory.
- ◇ Minimum 100µg of DNA for mutation analysis in the whole *DTDST* gene. Blood samples (minimum of 10 ml in EDTA) can also be sent to our laboratory by express mail (FedEx / UPS) at room temperature. Prenatal samples must be sent with parental samples. Please contact our laboratory (as above) for further details, including the minimal amount of DNA required for babies and small children.

#### Technical

- ◇ Mutation analysis by PCR amplification, enzymatic digestion and gel electrophoresis, and bi-directional fluorescent sequencing.

#### Target turn-round time

- ◇ Screening for frequent mild mutations in *DTDST* gene, or mutation analysis of the whole *DTDST* gene: -6-12 months. Prenatal diagnosis - only in families with known mutations: 1 - 2 weeks.
- ◇ 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

- ◇ Mutation analysis in an index case and parents: CHF 800 (€500) if the specimen is extracted DNA. Additional cost: CHF 50 (€30) if the specimen is a blood sample. In case the mutations are identified in the preliminary screening step (five most common mutations), and sequencing of the entire *DTDST* gene is not required, the cost of the test is reduced to CHF 200 (€125).
- ◇ Prenatal diagnosis: CHF 800 (€500). ADVANCE NOTICE IS MANDATORY.
- ◇ Carrier testing:
  - One single known mutation: CHF 100 (€60) if the specimen is extracted DNA. Additional cost: CHF 50 (€30) if the specimen is a blood sample.
  - Screening of the five most common mutations: CHF 200 (€125) if the specimen is extracted DNA. Additional cost: CHF 50 (€30) if the specimen is a blood sample.

#### References

- ◇ Superti-Furga A. *et al* (1999) *J Med Genet* **36**:621-4.
- ◇ Rossi A. *et al.* (2001) *Hum Mutat* **17**: 159-71.
- ◇ Ballhausen D. *et al.* (2002) Multiple Epiphyseal Dysplasia, Recessive. In: GeneReviews: Genetic Disease Online Reviews at GeneTests-GeneClinics [database online]. Copyright, University of Washington, Seattle. Available at <http://www.geneclinics.org>.

#### ESDN Administrator contact details

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

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