Molecular Genetics Service Profile
Diastrophic Dysplasia (DTD)

Introduction

◊ DTD (OMIM No. 222600) is an autosomal recessive disease characterized in the neonatal period by short limbed dwarfism, club feet and contractions of the hip, elbow and knee joints. The thumbs are typically short and radially deviated ("hitchhiker thumbs") and the great toe is often abducted. The skeletal changes are progressive. Degenerative arthrosis of the hip, severe lumbar lordosis, thoracolumbar kyphosis and scoliosis of the spine, flexion contractures of the knee, ulnar deviation, phalangeal synostosis and ankylosis of the hands frequently develop in older children and young adults.

◊ Radiological features include crescent-shaped, flattened epiphyses, shortening and metaphyseal widening of tubular bones, broadening of the cervical spine, cervical kyphosis, accessory ossification centres in the manubrium sterni.

◊ DTD is caused by mutations in the *DTDST* (*SLC26A2*) gene coding for a sulphate transporter.

Contact details for the laboratory carrying out the genetic test for DTD
Division of Molecular Pediatrics, Centre Hospitalier Universitaire Vaudois, Clinique Infantile 02-35 Av. Pierre Decker 2, CH-1011 Lausanne, Switzerland.
Dr. Luisa Bonafé. Tel: +41 21 314 3483. Fax: +41 21 314 3546. Email: laureane.mittaz-crettol@chuv.ch

Reasons for referral

◊ Mutation analysis in patients with a diagnostic suspicion of DTD on clinical and radiographic grounds.

◊ 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

◊ Minimum 100μg of DNA from peripheral lymphocytes or fibroblasts from your local laboratory. 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

◊ Mutation analysis of *DTDST* gene by sequencing: 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.

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.

◊ 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

◊ Hastbacka J. *et al*. (1994) Cell **78**: 1073-87.

◊ Superti-Furga A. *et al*. (1996) Am J Med Genet **63**: 144-7.

◊ Rossi A. *et al.* (2001) Hum Mutat **17**: 159-71.

ESDN Administrator contact details

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

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