

Molecular Genetics Service Profile Atelosteogenesis Type 2 (AO2)

Introduction

- ◇ AO2 (McAlister Dysplasia) (OMIM No. 256050) is a condition in the DTD dysplasia spectrum. It is intermediate in severity between achondrogenesis 1B (early lethal) and diastrophic dysplasia (non-lethal). Most cases of AO2 are not compatible with life either because of thorax hypoplasia and/or of cervical cord compression. Clinical and radiographic features are those of severe diastrophic dysplasia with short limbs, contractures at hips, knees and elbows, radial head dislocation, proximally deviated ("hitchhiker") thumbs clubfeet with sandal-gap between first and second toe. Cervical kyphosis is a frequent and severe; the distal humeri may be tapered; vertebral coronal clefts can be seen. The diagnostic suspicion can be confirmed by the finding of abnormal cartilage matrix (rarefaction of ground substance, coarse collagen fibres and collagen "rings" around chondrocytes) on histology.

Contact details for the laboratory carrying out the genetic test for AO2

Division of Molecular Pediatrics, Centre Hospitalier Universitaire Vaudois, Clinique Infantile 02-35 Av. Pierre Decker 2, CH-1011 Lausanne, Switzerland.

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Reasons for referral

- ◇ Mutation analysis in patients with a diagnostic suspicion of AO2 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.* (1996) *Am J Hum Genet* **58**:255-62.
- ◇ Rossi A *et al.* (1996) *Hum Genet* **98** :657-61.
- ◇ 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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