

## Molecular Genetics Service Profile Achondrogenesis Type 1B (ACG1B)

### Introduction

- ◇ ACG1B (OMIM No. 600972) is the most severe phenotype in the DTD dysplasia spectrum. Death occurs prenatally or shortly after birth. Clinical features include extremely short (flipper-like) limbs with short fingers and toes, proximal deviation of thumbs, clubfoot with sandal gap between 1st and 2nd toes, hypoplasia of the thorax, protuberant abdomen, and hydropic appearance caused by the abundance of soft tissue relative to the short skeleton. The face is flat, the neck is short with thickening of soft tissues. Useful radiographic signs are crescent-shaped, "paraglider-like" iliac bones and tubular bones that are very shortened and resembling "thorn apples" or "acanthocytes".
- ◇ ACG1B 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 ACG1B

**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](mailto:laureane.mittaz-crettol@chuv.ch)

### Reasons for referral

- ◇ Mutation analysis in patients with a diagnostic suspicion of ACG1B on clinical, radiographic, or histologic 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](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.
- ◇ 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.* (1996) *Nature Genet* **12**:100-2.
- ◇ Superti-Furga A. (1996) *J Med Genet* **33**:957-961.
- ◇ Rossi A. *et al.* (2001) *Hum Mutat* **17**: 159-71.
- ◇ Bonafé L. *et al.* (2002) Achondrogenesis type 1B. 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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