Molecular Genetics Service Profile
Achondrogenesis II and hypochondrogenesis (AII/H)

Introduction

◊ Achondrogenesis type II (MIM 200610) and hypochondrogenesis (MIM 120140.0002) are perinatally lethal skeletal dysplasias. They are not separate entities but represent rather a phenotypic spectrum at the most severe end of the type II collagenopathies. Affected infants are either stillborn or die soon after birth. Clinical manifestations include relatively large head, cleft palate, short neck, barrel-shaped chest with prominent abdomen and short limbs (Borochowitz Z *et al*, 1986).

◊ Radiographically the condition is characterized by variable lack of ossification of the vertebral bodies. The tubular bones are shortened with cupped metaphyses. The pelvis shows small iliac wings with concave medial and inferior margins.

◊ AII/H is caused by dominant mutations in the type II collagen gene (*COL2A1*) on 12q13 (Mortier GR *et al*, 1995 and 2000).

Contact details for the laboratory carrying out the genetic test for AII/H
Center for Medical Genetics Ghent (CMGG) Ghent University Hospital Medical Research Building (MRB), 2nd floor De Pintelaan 185, B-9000 Ghent, Belgium. http://medgen.ugent.be
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Reasons for referral

◊ Mutation analysis for confirmation of a radiographically/histologically suspected diagnosis of AII/H. Screening for unknown mutations is labour intensive, therefore we cannot accept urgent referrals of this type.

◊ Prenatal diagnosis is usually not requested since most cases are due to new mutations. In case of ultrasonographic evidence of recurrence within the same sibship (gonadal mosaicism in one of the parents), prenatal diagnosis can be offered if the mutation in the index case is known. However, we strongly recommend that this should only be offered within the context of genetic counselling

Samples

◊ Minimum 100μg of DNA from peripheral lymphocytes from your local laboratory. Blood samples (minimum of 5mls in EDTA) can also be sent to our laboratory by express mail (FedEx / UPS). Prenatal samples must be sent with a sample from both parents. For prenatal diagnosis: please contact our laboratory in advance.

Technical

◊ Mutation scanning of exons 1-54 of *COL2A1* by dHPLC. Fluorescent bidirectional sequencing of abnormal fragments.

Target turn-round time

◊ Mutation scanning of *COL2A1* – 3 months. Prenatal diagnosis – 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

◊ Full mutation screen - €1000.

References

◊ Borochowitz Z *et al*. (1986). *Am J Med Genet*. 24: 273-288.

◊ Mortier GR *et al*. (1995). *Hum Mol Genet.* **4**: 285-288.

◊ Mortier GR *et al*. (2000). *J Med Genet* **37**: 263-271.

ESDN Administrator contact details

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

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