Molecular Genetics Service Profile
Hypochondroplasia (HCH)

Introduction

◊ HCH (MIM 146000) is an autosomal dominant disease affecting 1 in 30,000 individuals. Clinical characteristics of HCH include mild dwarfism with large forehead, and absent or moderate macrocephaly. Radiographic features include reduced interpedicular distance between vertebral discs in the lower lumbar spine, metaphyseal flaring of tibiae and femurs, broad and short metacarpals and phalanges.

◊ HCH is caused mainly by recurrent mutations in the tyrosine kinase domains of the Fibroblast Growth Factor Receptor 3 (FGFR3), (Rousseau *et al*. 1996; Bellus *et al*. 2000). These mutations account for 60-65% of HCH cases.

Contact details for the laboratory carrying out the genetic test for HCH
Unité INSERM 781, Hopital Necker-Enfants Malades,149 rue de Sèvres, 75743 Paris, Cedex 15, France.
Dr. Laurence Legeai-Mallet. Tel:+33 1(01) 44 49 40 00 ext 97833. Fax:+33 1(01) 47 34 85 14.
Email: laurence.legeai-mallet@inserm.fr

Reasons for referral

◊ Mutation screening in patients with clinically confirmed or suspicion of HCH (sporadic or familial case).

◊ Differential diagnosis with dyschondrosteosis.

◊ Prenatal diagnosis is **not** offered for HCH.

Samples

◊ Minimum 20µg of DNA from peripheral blood from your local laboratory. Blood samples (minimum of 5mls in EDTA) can also be sent to our laboratory by express mail (Fed Ex or UPS). Blood samples from relatives are required in familial cases. Please contact our laboratory (as above) for further details.

Technical

◊ Mutation analysis by direct bi-directional sequencing of exons 13 and 15 of *FGFR3*.

Target turn-round time

◊ Routine analysis to confirm clinical diagnosis - 20 days. Screening for unknown mutations in other exons is labour intensive and will be performed only if solid clinical and radiological diagnosis of hypochondroplasia has been established. This may take several weeks (15-20 weeks) and may fail to reveal a *FGFR3* mutation. 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

◊ €200 for common mutations. €500 additional charge for unknown mutations.

References

◊ Rousseau F. *et al*. (1996) *J. Med. Genet*. **33**: 749-752

◊ Bellus G. *et al.* (2000) *Am. J. Hum. Genet*. **67**: 1411-1421

ESDN Administrator contact details

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

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