



MPHD
Autosomal dominant

www.endogenet.org

Molecular Genetics Service Profile

LHX4

Introduction

- ✓ The name LHX4 derives from LIM homeobox 4. The term LIM is an acronym of LIM11, IS11 and MEC3, which are all related transcription factors from different organisms, with similar DNA binding domains. It is a homeobox gene located on chromosome 1q25 and consists of six exons spread over 45 kb in total, encoding a protein of 367 amino acids.
- ✓ During the embryonic development the LHX4 protein is necessary for the correct expression of other pituitary transcription factors such as LHX3 and ISL1. Furthermore Rathke's pouch cells in mice need LHX4 for survival.
- ✓ Mutations within the LHX4 gene lead to autosomal dominant MPHD (Multiple Pituitary Hormonal Deficiency) with a very variable phenotype including **GH, TSH, PRL and ACTH**.
- ✓ MRI may show a hypoplastic pituitary gland, persistent craniopharyngeal canal or abnormal cerebellar tonsils (Arnold Chiari malformation).

Please photocopy and distribute this sheet as required

Reasons for referral

- ✓ Mutation screening in patients with clinically confirmed or suspected MPHD.

Samples

- ✓ Minimum of 2 ml blood sample in EDTA (or minimum of 50 µg DNA from peripheral lymphocytes) can be sent to our laboratory by express mail. In special cases a investigation of DNA from prenatal samples can be made, however you should contact our laboratory for further details.

Technical

- ✓ Mutation scanning of exons 1-6 of LHX4 by dHPLC (WAVE), denaturing high pressure liquid chromatography. Fragments with abnormal elution patterns are directly analyzed with Dideoxy sequencing (ABI 310).

Target turn-round time

- ✓ 3-4 weeks from the receipt of all required samples and clinical information.

Cost

- ✓ MPHD Full mutation screen (PROP1, POU1F1, HESX1, LHX3, LHX4) - € 1560. Screening the LHX4 gene is part of the **GeNeSIS** study sponsored by Eli Lilly and Company. Please contact your local representative. In special cases we will provide this service as part of our research program. Please contact us directly.

References

- ✓ Understanding the genetics of growth hormone deficiency. R.Pfäffle and W.F.Blum. (2000). TMG Healthcare Communications Ltd: 49-53.
- ✓ Machinis K et al. "Syndromic short stature in patients with a germline mutation in the LIM homeobox LHX4." Am J Hum Genet. 2001 Nov;69(5):961-8. Epub 2001 Sep 20.

Contact:

**Prof. Dr. Roland Pfäffle, University Hospital for Children and Adolescents, Oststr. 21-25, 04317 Leipzig.
Tel.: +49-341-9726123. Fax: +49-341-9726349. Email: rpfaeffle@medizin.uni-leipzig.de**