Molecular Genetics Service Profile

| GH1 (Growth Hormone 1 Gene) |

Introduction

- GH1 is part of a cluster of five related genes of about 66.5 kb in total on chromosome 17q23 and consists of five exons. The related genes are CSHP1, CSH1, CSH2 and GH2. Due to alternative splicing several isoforms of the encoded GH-protein (217 Aminoacids) exist with a molecular mass of 17.5 kDa to 22 kDa.
- The GH1 gene possesses some upstream regulatory elements that control its expression and a promoter with binding sites for the PIT1 Protein and other transcription factors.
- Mutations within the GH1 gene lead to IGHD (Isolated Growth Hormone Deficiency) of three different types:
  - Autosomal recessively inherited IGHD type 1A due to deletions of heterogeneous length and substitution mutations. Phenotype with completely absent GH, severe short stature and often Anti-GH antibodies upon treatment.
  - Autosomal recessively inherited IGHD type 1B due to mutations in the GH1 gene or splice sites (NS4). Phenotype with a less active GH protein, short stature and a good response to GH treatment.
  - Autosomal dominant inherited IGHD type 2 due to splice site mutations. Phenotype with an impaired GH secretion from pituitary secretory vesicles, short stature and a good response to GH treatment.

Reasons for referral

- Mutation screening in patients with clinically confirmed or suspected IGHD.

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 1-5 of GH1 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

- IGHD Full mutation screen (GH1 and GHRHR) - € 1080. Screening the GH1 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


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