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**Holoprosencephaly
Autosomal dominant**

Molecular Genetics Service Profile **SHH (HHG-1)**

Introduction

- ✓ The term SHH derives from an acronym of Sonic Hedgehog, one of three homologs of the *Drosophila* gene *hh* (hedgehog). The SHH gene has been mapped to chromosome 7q36, spans 9.41 kb, and consists of 3 exons, which encode a predicted protein of 462 amino acids.
- ✓ SHH is important for the early embryonic development of the neural plate, the limbs, the hematopoietic cells, the retina and other organs. Therefore the phenotype of SHH mutations is very variable.
- ✓ Mutations within the SHH gene may lead to autosomal dominantly inherited **holoprosencephaly** of varying degree.
- ✓ Other clinical features: **Midline defects (with pituitary anomalies and IGHD or MPHD), solitary median maxillary central incisor, ocular coloboma, maybe oesophageal atresia and/or cleft palate.**

Please photocopy and distribute this sheet as required

Reasons for referral

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

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 1-3 of SHH 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

- ✓ Mutation screen (SHH) - € 240. In special cases we will provide this service as part of our research program. Please contact us directly.

References

- ✓ Nanni L et al. "The mutational spectrum of the sonic hedgehog gene in holoprosencephaly: SHH mutations cause a significant proportion of autosomal dominant holoprosencephaly." *Hum Mol Genet.* 1999 Dec;8(13):2479-88.

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