

## Pallister-Hall Syndrome Testing via *GLI3* Gene Sequencing (Test #380)

**Brief Description of Clinical Features:** Pallister-Hall Syndrome (PHS) (OMIM 146510) is characterized by hypothalamic hamartoma with or without gelastic seizures, polydactyly, nail displasia, imperforate anus, bifid epiglottis, and laryngotracheal clefts. PHS patients may have pituitary insufficiency which can result in death from adrenal insufficiency. Symptoms are variable in appearance and severity. Inter-familial variability has been reported to be much greater than intra-familial variability. For more information see Biesecker GeneReviews 2006 (<http://www.geneclinics.org/>).

**Genetics:** PHS is caused by mutations in the *GLI3* gene on chromosome 7p (Kang et al. Nat Genet 15:266-268, 1997; Johnston et al. Am J Hum Genet 76:609-622, 2005). Mutations either occur *de novo* or are inherited dominantly. The fraction of patients with *de novo* mutations is unknown. PHS mutations are mostly (possibly even entirely) truncating (nonsense, frameshift, and obvious splicing defects) and are usually located within the middle third of the gene (Johnston et al. 2006). No mutations are predominant. *GLI3* is the only gene that has been implicated in PHS.

**Description of This Particular Test:** This test involves bidirectional sequencing of the coding regions of all 14 coding *GLI3* exons plus about 50 bp of non-coding flanking DNA on each side (Wild et al. Hum Mol Genet 6:1979-1984, 1997). The large exon 14 (2311 bp coding region) is sequenced as five overlapping fragments.

**Indications for Test:** All patients with symptoms consistent with PHS are candidates for this test. We will sequence single, specified exons in family members of patients with known mutations and in research subjects to confirm research results. Mutations within *GLI3* may also cause Postaxial Polydactyly Type A and Preaxial Polydactyly Type IV.

**Sensitivity of Test:** Johnston et al. 2006 reported that 95% of PHS patients carry mutations in the coding regions of *GLI3*.

**Turn Around Time:** Maximum of 40 days. Many tests, however, are completed in 2-3 weeks.

**Specimen Requirements:** See page 4 of the Requisition Form.

**Price:** Sequence analysis of the *GLI3* gene **\$1,090**

**CPT Codes:**

Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification X18	83898	\$ 370	Mutation Ident by Sequencing X18	83904	\$ 500
Separation	83894	\$ 60	Interpretation and Report	83912	\$ 90

**Single exon sequencing is available for \$190.**

**Accreditation Info.** CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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