**HESX1 Gene Analysis in Septo-Optic Dysplasia**

*Also known as:* pituitary hormone deficiency-5; CPHD5 and as growth hormone deficiency with pituitary anomalies

*Mendelian Inheritance in Man Number:* 601802 (HESX1 gene), 182230 (Septooptic Dysplasia)

**Clinical features:**
Septo-optic dysplasia (SOD) is a disorder of early brain development with a variable phenotype. The diagnosis of this disorder is established by the presence of any combination of optic nerve hypoplasia, pituitary gland hypoplasia, and midline brain abnormalities. The brain abnormalities include absence of the corpus callosum and septum pellucidum (Dattani, 1998). About one-third of people diagnosed with septo-optic dysplasia have all three major features; most affected individuals have two of the major features.

Mutations in the HESX1 gene have also been identified in patients with combined pituitary hormone deficiency without other abnormalities being present (Sobrier, 2006).

*Inheritance pattern:*
Autosomal recessive and autosomal dominant with incomplete penetrance

**Reasons for referral:**
1. Confirmation of a clinical diagnosis
2. Development of an appropriate management plan
3. Genetic counseling
4. Prenatal diagnosis in families with a defined mutation

**Test method:**
Using genomic DNA obtained from the submitted biological material, bi-directional sequencing of all four exons and their respective splice sites of the HESX1 gene is performed. Mutations found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis, or another appropriate method.

**Test sensitivity:**
McNay et al., identified a mutation in the HESX1 gene in less than 1% of a cohort of 861 patients (724 sporadic, 126 familial, and 11 consanguineous) presenting phenotypes ranging from the complete SOD triad to any one part of the triad (McNay 2007). In another study the HESX1 gene was sequenced in 105 patients with the complete SOD triad, 85 patients with isolated pituitary hypoplasia, and 38 patients with holoprosencephaly or a related disorder. This study reported 1 mutation in the SOD cohort (~1%) and 3 mutations in the cohort with isolated pituitary hypoplasia (~3.5%) (Thomas 2001).
**Mutation spectrum:**
Of the 13 mutations published thus far, 8 are missense, 3 are frameshift, 1 is a splice site mutation, and 1 is an insertion of a 300bp Alu repeat segment.

**Specimen Requirements and Shipping/Handling:**
- **Blood:** A single tube with 1-5 mL whole blood in EDTA. Ship overnight at ambient temperature, using a cool pack in hot weather. Specimens may be refrigerated for 7 days prior to shipping.
- **Buccal Brushes:** Can be used as an alternative to blood. When sending a buccal sample, use a GeneDx buccal kit (others not accepted). Submit by mail. Buccal brushes are not accepted on children less than 6 months of age.
- **Prenatal Diagnosis:** 10 mL amniotic fluid, 5 mg CVS, or 2 T25 flasks. Ship overnight at ambient temperature, using a cool pack in hot weather. Call to discuss requirements for parental blood. Keep backup cultures.

**Required Forms:**
- Sample Submission (Requisition) Form – complete all pages
- Payment Options Form or Institutional Billing Instructions

**Prices and Turn-Around Time - Fees are subject to change without notice:**
Test # 474: Mutation detection in a new patient = $530; Approximately 5-6 weeks
Test # 9011: Testing of a relative for a specific known mutation = $350; Approximately 2-4 weeks
Test # 9012: Testing of a relative for two specific known mutations = $500; Approximately 2-4 weeks
Test # 902: Prenatal diagnosis for a specific known mutation = $2000; Approximately 2 weeks

*Please see our website for CPT codes/prices for ExonArrayDx, carrier and prenatal testing:
www.genedx.com

**CPT codes for mutation detection in a new patient - All codes and units apply:**

Test # 474: Sequencing of the HESX1 gene

83891 x 3 units
83898 x 6 units
83894 x 3 units
83904 x 6 units
83892 x 2 units
83912 x 2 units

**TOTAL $ 530**

**Possible ICD9 Codes:**
Optic nerve hypoplasia: 377.43