Hermansky-Pudlak Syndrome: HPS4 Gene Deletion/Duplication

Test Code: DHPS4  
Turnaround time: 2 weeks  
CPT Codes: 81228 x1

**Condition Description**

Hermansky-Pudlak syndrome (HPS) is an autosomal recessive, multisystemic disorder. The main clinical features of HPS include oculocutaneous albinism which presents as hypopigmentation of the skin and hair; reduced iris and retinal pigments; loveal hypoplasia; nystagmus; and increased crossing of optic fibers; bleeding diathesis due to a platelet storage pool deficiency; and deposition of lysosomal ceroid, which may cause pulmonary fibrosis (onset in the early thirties), granulomatous colitis (severe presentation in ~ 15% of all cases) and cardiomyopathy in some cases. The clinical features of HPS are caused by the disruption of lysosome-related organelles in different tissue types. The incidence of HPS is approximately 1 in 500,000-1,000,000. HPS has an increased incidence, of up to 1 in 1800, in Puerto Rico. Locus heterogeneity has been associated with HPS and nine causative genes (HPS1-HPS9) have been identified to date. Pathogenic variants in the HPS4 (22q12.1) gene, account for approximately 12% of all cases in non-Puerto Rican populations.

**References:**
- GeneReviews
- Wei & Li (2013). Pigm Cell Melanoma R, 26:176-192
- OMIM #614073: HPS
- OMIM #606682: HPS4 gene

**Indications**

This test is indicated for:
- Confirmation of a clinical diagnosis of HPS in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of HPS in whom sequence analysis was negative.

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic pathogenic variants. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

**Type: Whole Blood**

Specimen Requirements:
- In EDTA (purple top) tube:
  - Infants (2 years): 3-5 ml
  - Older Children & Adults: 5-10 ml
- Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:
Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Special Instructions**

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the *HPS4* gene is available and is required before deletion/duplication analysis.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.