## 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, 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.

Mutations in the HPS1 (10q24.2) gene are responsible for approximately 45% of all cases in non-Puerto Rican populations. In Puerto Ricans, a 16bp duplication (c.1470_1486dup), in the HPS1 gene, causes 75% of all cases. Please note that this test is for the HPS1 gene only, so mutations in the HPS2-HPS9 genes will not be identified.

### References:

- GeneReviews
- Wei & Li (2013). Pigm Cell Melanoma R, 26:176-192
- OMIM #203300: HPS
- OMIM #604982: HPS1 gene

## Genes

**HPS1**

## Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Hermansky-Pudlak syndrome.
- Carrier testing in adults with a family history of Hermansky-Pudlak syndrome.

## Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### Detection

**Clinical Sensitivity:** Sequencing can detect approximately 45% and 75% of cases in the non-Puerto Rican and the Puerto Rican populations respectively. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Analytical Sensitivity:** ~99%

## Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Related Tests**

- 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.