### 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; foveal hypoplasia; nystagmus; 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.

Pulmonary fibrosis is a condition in which the lung tissue becomes thickened and scarred over time making the lungs incapable of transporting oxygen into the bloodstream effectively. The most common signs and symptoms of idiopathic pulmonary fibrosis are shortness of breath and a persistent dry, hacking cough. Many affected individuals also experience a loss of appetite and gradual weight loss. It is reported that about 0.5-3.7% of idiopathic pulmonary fibrosis is familial.

### References
- GeneReviews.
- OMIM #203300: HPS.

### Genes

- **ABCA3**
- **AP3B1**
- **BLOC1S3**
- **BLOC1S6**
- **CSF2RA**
- **DTNBP1**
- **ELMOD2**
- **HPS1**
- **HPS3**
- **HPS4**
- **HPS5**
- **HPS6**
- **SFTPB**
- **SFTPC**
- **SFTPDL**
- **TERT**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of pulmonary fibrosis.
- Confirmation of a clinical diagnosis 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

#### Next Generation Sequencing:
Clinical Sensitivity: Unknown. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

### 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: Ship sample at room temperature with overnight delivery.
Type: Isolated DNA

Specimen Requirements:

In microtainer: 60 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

Related Tests

- Pulmonary Disease Comprehensive Panel
- Pulmonary Arterial Hypertension Panel
- Bronchiectasis
- Cystic Lung Disease Panel
- Congenital Central Hypoventilation Syndrome Panel
- HPS1 Gene Sequencing
- HPS4 Gene Sequencing
- HPS4 Deletion/Duplication Panel
- Pulmonary Fibrosis and Hermansky-Pudlak Syndrome: Deletion/Duplication Panel