Hermansky-Pudlak Syndrome: \textit{HPS1} Gene Sequencing

\textbf{Test Code:} SHPS1  
\textbf{Turnaround time:} 4 weeks  
\textbf{CPT Codes:} 81479 $x_1$

\section*{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 (\textit{HPS1-HPS9}) have been identified to date.

Mutations in the \textit{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 \textit{HPS1} gene, causes 75% of all cases. Please note that this test is for the \textit{HPS1} gene only, so mutations in the \textit{HPS2-HPS9} genes will not be identified.

\section*{References:}
- OMIM \#203300: HPS
- OMIM \#604982: \textit{HPS1} gene

\section*{Genes}
\textit{HPS1}

\section*{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.

\section*{Methodology}

\textbf{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.

\section*{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%

\section*{Specimen Requirements}

\textit{Submit only 1 of the following specimen types}

\section*{Type: DNA, Isolated}

\textbf{Specimen Requirements:}
- Microtainer
- 8µg
- Isolation using the Perkin Elmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

\textbf{Specimen Collection and Shipping:}
- Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

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Type: Whole Blood (EDTA)

Specimen Requirements:
EDTA (Purple Top)
Infants and Young Children (< 2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

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

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.