

Peroxisome Biogenesis Disorders, Zellweger Syndrome Spectrum, *PEX5*-related: *PEX5* Gene Sequencing

Test Code: SPEX5

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

Peroxisome biogenesis disorders, Zellweger syndrome spectrum (PBD, ZSS) is a continuum that encompasses three distinct phenotypes; Zellweger syndrome (ZS), neonatal adrenoleukodystrophy (NALD), and infantile Refsum disease (IRD). Individuals with PBD, ZSS usually present during the newborn period or later in childhood. Features during the newborn period include hypotonia, poor feeding, distinctive facial features, seizures, and liver cysts with hepatic dysfunction. Infants with ZS, the most severe phenotype on the spectrum, are significantly impaired and usually do not survive past the first year of life. Those that do survive past the first year have developmental delay with hypotonia, liver dysfunction, sensorineural hearing loss, and retinal dystrophy. Features of NALD and IRD (the least severe phenotype on the spectrum) are variable. They include developmental delays, liver dysfunction, episodes of intracranial bleeding, hearing loss, and vision impairments. PBD, ZSS can be slowly progressive.

PBD, ZSS is inherited in an autosomal recessive manner. Biochemical assays can definitively diagnose PBD, ZSS. Mutations in twelve different *PEX* genes have been identified to cause PBD, ZSS. They are the *PEX1*, *PEX2*, *PEX3*, *PEX5*, *PEX6*, *PEX10*, *PEX12*, *PEX13*, *PEX14*, *PEX16*, *PEX19*, and *PEX26* genes. About 68% of individuals with PBD, ZSS have mutations in the *PEX1* gene. Mutations in the *PEX6*, *PEX10*, *PEX12*, and *PEX26* genes account for an additional 26% of mutations in individuals with PBD, ZSS.

Please note that this test is for the *PEX5* gene (12p13.3) only.

For patients with suspected PBD, ZSS, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

References:

- GeneReviews
- [OMIM #600414](#): *PEX5* gene
- [OMIM #214100](#): ZS

Genes

[PEX5](#)

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of peroxisome biogenesis disorders, Zellweger syndrome spectrum.
- Carrier testing in adults with a family history of peroxisome biogenesis disorders, Zellweger syndrome spectrum.

Methodology

PCR amplification of 15 exons contained in the *PEX5* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

Detection

Clinical Sensitivity: Mutations in the *PEX5* gene account for ~1.5% of individuals with PBD, ZSS. 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

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.

Type: DNA, Isolated**Specimen Requirements:**

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

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.

Special Instructions

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Related Tests

- Deletion/duplication analysis of the *PEX5* gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Sequence and deletion/duplication analysis for the *PEX1*, *PEX2*, *PEX3*, *PEX6*, *PEX12*, *PEX14* and *PEX26* genes are also available.
- 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.