

PRPS1-related Disorders: PRPS1 Gene Deletion/Duplication

Test Code: DPRPS

Turnaround time: 2 weeks

CPT Codes: 81228 x1

Condition Description

Mutations in the *PRPS1* gene (Xq22-q24) can result in one of four X-linked syndromes: phosphoribosylpyrophosphate synthetase-1 (PRPS1) superactivity, Charcot-Marie-Tooth disease-5 (CMTX5), Arts syndrome, and X-linked nonsyndromic sensorineural deafness (DFN2). Affected individuals may have neurological, hematopoietic and/or purine overproduction symptoms. Neurological symptoms can include ataxia, hypotonia, optic atrophy, hearing impairment, and neuropathy. The main hematopoietic symptom can be susceptibility to infection. Purine overproduction symptoms manifest primarily as uric acid stones, hyperuricemia, and gout. Phenotype may vary both between and within families.

PRPS1 Superactivity

The clinical presentation of PRPS1 superactivity is variable. Individuals may present in early adulthood with hyperuricemia and hyperuricosuria. Uric acid overproduction may be accompanied by intellectual disability, ataxia, hypotonia, and hearing impairment. Some female carriers have been reported to be symptomatic, with hyperuricemia, gout, and hearing impairment.

Charcot-Marie-Tooth Disease-5

Charcot-Marie-Tooth disease-5 (CMTX5) is defined by peripheral neuropathy, early-onset sensorineural hearing impairment, and optic atrophy. Hypotonia, gait disturbances, and loss of deep tendon reflexes develop around age 10 to 12 years, likely due to peripheral demyelination and axonal loss. Intellectual disability is not a feature of CMTX5. Some carrier females have been reported to have hearing impairment while others are unaffected.

Arts Syndrome

Arts syndrome is characterized by intellectual disability, early-onset hypotonia, ataxia, delayed motor development, profound congenital sensorineural hearing impairment, and optic atrophy. Susceptibility to infections, especially of the upper respiratory tract, can result in early death. Carrier females may show isolated and milder symptoms.

X-Linked Nonsyndromic Sensorineural Deafness

Individuals with X-linked nonsyndromic sensorineural deafness (DFNX1 or DFN2) generally present with postlingual progressive nonsyndromic hearing loss, although one family has been reported with congenital profound nonsyndromic hearing loss. Female carriers are reported to have mild to moderate hearing loss.

For patients with suspected *PRPS1*-related disorders, 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:

- [OMIM #300661](#): Phosphoribosylpyrophosphate Synthetase Superactivity.
- [OMIM #311070](#): Charcot-Marie-Tooth Disease, X-Linked Recessive, 5; CMTX5.
- [OMIM #301835](#): Arts Syndrome; ARTS.
- [OMIM #304500](#): Deafness, X-Linked 1; DFNX1.
- Arjan, PM et al. PRPS1 Mutations: Four Distinct Syndromes and Potential Treatment. American Journal of Human Genetics 2010; 86:506-518.

Genes

[PRPS1](#)

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of *PRPS1*-related disorders in an individual in whom sequence analysis was negative.
- Carrier testing in adult females with a family history of autosomal recessive *PRPS1*-related disorders in an individual 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.

Detection

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

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:

Microtainer

3µg

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.

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 *PRPS1* gene is available and is required before deletion/duplication analysis.
- A next-generation sequence analysis panel of 90+ XLID genes is available.
- A CGH array-based test for deletion/duplication analysis of 90+ XLID genes is available.
- 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.