

Renpenning Syndrome 1: *PQBP1* Gene Sequencing

Test Code: YP

Turnaround time: 4 weeks

CPT Codes: 81405 x1

Condition Description

Mutations in the *PQBP1* gene (Xp11.23) cause X-linked recessive mental retardation that is often syndromic but can be nonsyndromic. *PQBP1* mutations have been associated with Renpenning syndrome, Sutherland-Hann syndrome, cerebropalatocardiac (Hamel) syndrome, and Golabi-Ito-Hall syndrome. Common features of X-linked mental retardation caused by *PQBP1* mutation seem to be mental retardation, microcephaly, and short stature. Considerable phenotypic variability is observed between families with different mutations and even between families with the same mutation.

In addition to mental retardation, microcephaly, and short stature, other reported features include small testes, ocular colobomas, cardiac malformations, cleft palate, spastic diplegia, and anal anomalies. Facial characteristics include narrow and tall craniofacies with upslanting palpebral fissures, abnormal nasal configuration, cupped ears, and short philtrum. The nose may appear long and bulbous, with overhanging columella.

Historically, Renpenning syndrome has been associated with mental retardation with short stature, moderate microcephaly, but no remarkable facies and no other neurologic abnormalities. Sutherland-Hann syndrome has been associated with mental retardation, short stature, microcephaly, brachycephaly, spastic diplegia, small testes, and possibly intrauterine growth retardation. Cerebropalatocardiac (Hamel) syndrome has been associated with severe mental retardation with congenital heart defects, microcephaly, spasticity, short stature, cleft or highly arched palate, and other craniofacial abnormalities. Golabi-Ito-Hall syndrome has been associated with mental retardation, microcephaly, postnatal growth deficiency, and other anomalies, including atrial septal defect.

For patients with suspected Renpenning syndrome, 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.

[Click here](#) for the OMIM summary on this condition.

Genes

[PQBP1](#)

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of Renpenning syndrome
- Carrier testing in adult females with a family history of Renpenning syndrome

Methodology

PCR amplification of 6 exons contained in the *PQBP1* 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: Unknown. 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 biochemical phenotype.

Analytical Sensitivity: ~99%

Specimen Requirements

Submit only 1 of the following specimen types

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.

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.

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

- Deletion/duplication analysis of the *PQBP1* gene by CGH array is available for those individuals in whom sequence analysis is negative (YQ).
- A CGH array-based test for deletion/duplication analysis of 64 different X-linked intellectual disability genes is available (OL).
- [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 to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.