

Assay Summary

PQBP1 Gene Mutation Analysis

Non-Syndromic X-Linked Mental Retardation, Renpenning syndrome, Sutherland-Haan syndrome and cerebropalatocardiac (Hamel) syndrome

Synopsis

X-linked mental retardation (XLMR) has a prevalence of 2.6 cases per 1,000 in the general population¹. Recently, mutations in the PQBP1 gene have been found in association with both non-syndromic XLMR and syndromic XLMR: i) Renpenning syndrome (mental retardation with short stature, moderate microcephaly, but no remarkable facies and no other neurologic abnormalities); ii) Sutherland-Haan syndrome (mental retardation, short stature, microcephaly, brachycephaly, spastic diplegia, small testes, and possibly intrauterine growth retardation); iii) Cerebropalatocardiac (Hamel) syndrome (severe mental retardation with congenital heart defects, microcephaly, spasticity, short stature, cleft or highly arched palate, and other craniofacial abnormalities)^{2,3} and iv) Golabi-Ito-Hall syndrome (mental retardation, microcephaly, postnatal growth deficiency, and other anomalies, including atrial septal defect⁴).

Indications for testing

Individuals with a diagnosis of non-syndromic mental retardation, especially those in whom Fragile X disease has been ruled out, or individuals with a diagnosis of Renpenning syndrome, Sutherland-Haan syndrome, or cerebropalatocardiac (Hamel) syndrome are candidates for testing. After a specific mutation is identified in a family, carrier testing can be performed for appropriate at-risk females and presymptomatic males. With appropriate genetic counseling, prenatal testing can be performed for females with an identified mutation.

Methodology

Full Mutation Analysis of PQBP1: All six coding exons and associated intron junctions of the PQBP1 gene are analyzed by direct DNA sequence analysis using an automated fluorescent sequencing machine. When a mutation is detected, confirmation is carried out by sequencing in the opposite direction, in an independent PCR amplification. If no mutation is found sequence analysis is performed in both directions. At-risk family members can be offered DNA sequence analysis of only the region of the gene with the previously identified mutation.

Limitations

For mutation analysis, the method will not detect mutations located in regions of the genes that are not analyzed (non-coding exon regions, intron regions other than the splice junctions, and upstream and downstream regions). The method also will not detect gross genetic alterations including most large deletion in female, duplications, and inversions. Some sequence alterations that may be detected (such as those causing missense or synonymous changes) will be of unknown clinical significance. Interpretation of test results should be in the context of the patient's ethnicity, clinical and family histories, and other laboratory test results.

Specimen Requirements

- (a) Blood samples: 2 tubes with a total of 6 ccs in ACD (yellow top) or EDTA (lavender top) tubes. Keep at ambient temperature and ship by overnight courier. Samples must be received in our laboratory within 72 hours of draw.

Note:

- i) for infants, a minimum of 3 ccs is sufficient.
- ii) we accept DNA; at least 10 micrograms is required.

- (b) Prenatal samples: 2 T25 flasks of confluent cells sent padded to arrive on M/Tu/W. A blood sample from the mother maybe required (2 tubes with a total of 6 ccs in ACD (yellow top) or EDTA (lavender top) tubes) for use as positive control. Maternal cell contamination studies are not done here but are required for autosomal disorders and dosage analysis on X-linked disorders. We would be happy to assist in coordinating sending out a specimen for this purpose.

Test Request Form (TRF)

A completed MDL [TRF](#) is required for each specimen. Please submit the completed TRF with the specimen. Complete testing and billing information must be provided before the specimen is processed.

<i>Order Codes</i>	<i>CPT Codes</i>	<i>TAT</i>
PQBP1-SEQ (PQBP1 gene, full gene sequencing)	83890, 83898(x6), 83894, 83904(x6), 83912	5 wks
PQBP1-CAS (PQBP1 gene, targeted mutation analysis, known mutation)	83890, 83898, 83894, 83904, 83912	3 wks
PQBP1-PD (PQBP1 gene, known mutation detection, prenatal)	83890, 83898, 83894, 83904, 83912	2 wks

References

1. Stevenson RE, Schwartz CE (2002). *Cytogenet Genome Res.* 99(1-4):265-75.
2. Kalscheuer VM, et al. (2003). *Nature Genet.* 35: 313-315.
3. Lenski C, et al. (2004). *Am. J. Hum. Genet.* 74: 777-780.
4. Lubs H. et al. (2006) *J Med Genet.* 43:e30

NOTE: This test is performed pursuant to a license agreement with Roche Molecular Systems, Inc.