Renpenning Syndrome 1: \textit{PQBP1} Gene Deletion/Duplication

\textbf{Condition Description}

Mutations in the \textit{PQBP1} gene (Xp11.23) cause \textit{X}-linked recessive mental retardation that is often syndromic but can be non-syndromic. \textit{PQBP1} mutations have been associated with Renpenning syndrome, Sutherland-Hann syndrome, cerebropalatocardiac (Hamel) syndrome, and Golabi-Ito-Hall syndrome. Common features of \textit{X}-linked mental retardation caused by \textit{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 or 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.

\textbf{Genes}

\textit{PQBP1}

\textbf{Indications}

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of Renpenning syndrome in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of Renpenning syndrome who have tested negative for sequence analysis

\textbf{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.

\textbf{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.

\textbf{Specimen Requirements}

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

\textbf{Type: DNA, Isolated}

\textbf{Specimen Requirements:}
- Microtainer
- 3µg
- Isolation using the Perkin Elmer™ 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.

\textbf{Type: Whole Blood (EDTA)}

\textbf{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

\textbf{Specimen Collection and Shipping:}
- Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or 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

- Sequencing analysis of the PQBP1 gene is available (YP) and is required before deletion/duplication analysis.
- ACGH array-based test for deletion/duplication analysis of 64 different X-linked intellectual disability genes is available (OL).
- 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.