XLMR 94: GRIA3 Gene Deletion/Duplication

Test Code: DGRI3
Turnaround time: 2 weeks
CPT Codes: 81228 x1

Condition Description

Mutations in the GRIA3 gene (Xq25-q26) (OMIM# 305915) have been associated with syndromic X-linked intellectual disability (XLID) (OMIM# 300699). In a study of 400 males with XLID who had a normal karyotype and negative fragile X testing, missense GRIA3 mutations were found in four males and a 0.4 Mb deletion of the GRIA3 gene was found in 3 males. Phenotypic features common in the males with GRIA3 mutations included moderate intellectual disability, poor muscle bulk, muscle weakness, asthenic body habitus, and hyporeflexia. Other features included seizures, macrocephaly, myoclonic jerks, and autistic behavior.

A partial duplication of the GRIA3 gene was also reported in a family with X-linked intellectual disability. Two affected brothers had delayed psychomotor development with severely delayed and poor language acquisition. One of the brothers also had dysmorphic features and fits of anger. The mother of the affected individuals displayed facial hypotonia, language and learning disabilities and a moderately short upper lip. An apparently balanced t(X;12)(q24;q15) translocation that disrupted the GRIA3 gene was identified in a woman with intellectual disability, bipolar disorder, seizures, and cyclic vomiting. A partial tandem duplication of exons 1-6 of the GRIA3 gene was found in a boy with nonsyndromic intellectual disability. His carrier mother was unaffected.

For patients with suspected GRIA3-Related- XLMR, 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# 305915: GRIA3 gene
- OMIM# 300699: XLMR 94

Genes

GRIA3

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of XLMR 94 in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of XLMR 94 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.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

Detection

Detection is limited to duplications and deletions. In a study of 400 males with XLID who had a normal karyotype and negative fragile X testing, missense GRIA3 mutations were found in four males and a 0.4 Mb deletion of the GRIA3 gene was found in 3 males. 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

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Related Tests**

- Sequence analysis of the \textit{GRIA3} gene is available and is required before deletion/duplication analysis.
- 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.
- \textit{X-Linked Intellectual Disability} panels are available for 30, 60, and 90 genes.