Glycerol Kinase Deficiency: GK Gene Deletion/Duplication

Test Code: DGKX1
Turnaround time: 2 weeks
CPT Codes: 81228 x1

Condition Description

Intellectual disability (ID) is a nonprogressive cognitive impairment affecting 1-3% of the Western population. It is estimated that up to 50% of moderate-severe cases have genetic causes and approximately 10% are due to X-linked intellectual disability disorders (XLID). XLID can be syndromic or nonsyndromic and is observed in all ethnic groups. More than 100 XLID syndromes have been described in the literature to date. Fragile X is the most common XLID syndrome (~1 in 4000 males) while others can be quite rare with only a few patients reported in the literature. Males can have moderate to severe intellectual disability depending on the syndrome, and carrier females can also be affected, but typically have milder clinical symptoms.

Mutations and deletions of the GK gene (Xp21.3) cause glycerol kinase deficiency (GKD). GKD can be part of a contiguous gene syndrome or occur as isolated GKD. The isolated form can either be symptomatic or asymptomatic. Isolated symptomatic GKD presents in early childhood with episodes of metabolic (vomiting and acidosis) and central nervous system (CNS) (lethargy and coma) decompensation. Additionally, individuals with the symptomatic GKD were reported to have intellectual disability, developmental delay, and/or seizures. Isolated asymptomatic GKD presents with hyperglycerolemia and glyceroluria but do not have the episodes of metabolic and CNS decompensation.

Complete loss of GK activity, caused by GK gene deletions and nonsense mutations, is typically associated with the symptomatic form of GKD. GK gene missense mutations that result in residual GK enzyme activity may or may not result in the symptomatic form of GKD.

GKD as part of a contiguous gene syndrome can include the DAX1 gene, which is responsible for adrenal hypoplasia congenital, the DMD gene, which causes Duchenne muscular dystrophy, and/or the OTC gene, which is responsible for ornithine transcarbamylase deficiency. The contiguous gene syndrome can be detected by array comparative genomic hybridization (aCGH).

References:
- OMIM #300474: GK gene
- OMIM #307030: GKD

Genes

GK

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of Glycerol Kinase Deficiency in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of Glycerol Kinase Deficiency 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. 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) or ACD (yellow 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.

**Special Instructions**

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the GK gene is available and is required before deletion/duplication analysis.
- Chromosomal Microarray EmArray 60K
- 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.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90 genes.