Intellectual Disability, DLG3-related: DLG3 Gene Deletion/Duplication

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

Condition Description

Mutations in the DLG3 gene have been shown to cause non-syndromic intellectual disability. Non-syndromic intellectual disability patients do not manifest other clinical signs.

DLG3 encodes synapse-associated protein 102 (SAP102), a member of the membrane-associated guanylate kinase protein family. Neuronal SAP102 is expressed during early brain development and is localized to the postsynaptic density of excitatory synapses. It is composed of three amino-terminal PDZ domains, a src homology domain, and a carboxyl-terminal guanylate kinase domain. The PDZ domains interact directly with the NR2 subunits of the NMDA glutamate receptor and with other proteins responsible for NMDA receptor localization, immobilization, and signaling. NMDA receptors have been implicated in the induction of certain forms of synaptic plasticity, such as long-term potentiation and long-term depression, and these changes in synaptic efficacy have been proposed as neural mechanisms underlying memory and learning. The disruption of NMDA receptor targeting or signaling, as a result of the loss of SAP102, may lead to altered synaptic plasticity and may explain the intellectual impairment observed in individuals with DLG3 mutations.

For patients with suspected DLG3-related intellectual disability, 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.

Genes

DLG3

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of DLG3-related intellectual disability in an individual in whom sequencing analysis was negative.
- Carrier testing in adult females with a family history of DLG3-related intellectual disability in whom sequencing 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 mutations 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

Please submit copies of diagnostic biochemical test results along 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 Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition form.

Related Tests

- DLG3-Related Intellectual Disability: DLG3 Gene Sequencing (SY) is required before deletion/duplication analysis.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.