HSD17B10-related Disorders: HSD17B10 Gene Deletion/Duplication

Test Code: DHSD1
Turnaround time: 2 weeks
CPT Codes: 81228 x1

Condition Description

Intellectual disability (ID) is a non-progressive 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 in the HSD17B gene (Xp11.22) also referred to as HADH2 can cause syndromic X-linked mental retardation 10, X-linked mental retardation 17, or 2-methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency.

Syndromic X-Linked Mental Retardation 10
Reyniers et al. described five patients from a four generation family who had mild intellectual disability and neurological symptoms. The neurological features included abnormal behavior and choreoathetosis. Choreoathetosis is the most distinguishing feature in individuals with this syndrome. It is characterized by chorea, which is involuntary, irregular, purposeless, nonrhythmic, abrupt, rapid movements, blended with athetosis, which is slow, writhing, continuous movements. Behavioral abnormalities included aggression, agitation, hallucination, and self mutilation. Carrier females were unaffected. Lenski et al. identified a mutation in HSD17B10 in affected family members that results in decreased protein expression.

X-Linked Mental Retardation 17
Microduplications of chromosome Xp11.22, including both the HSD17B10 and the HUWE1 genes, cause a nonsyndromic form of X-linked intellectual disability (X-Linked Mental Retardation 17). The intellectual disability is mild to moderate in severity.

2-Methyl-3-Hydroxybutyryl-CoA Dehydrogenase Deficiency
2-Methyl-3-hydroxybutyryl-CoA dehydrogenase (MHBD) deficiency, also called 17-beta-hydroxysteroid dehydrogenase X deficiency, is an X-linked inborn error of isoleucine metabolism. MHBD deficiency is characterized by progressive loss of mental and motor skills following normal early development. The most common clinical feature is speech delay. Other common symptoms include visual and hearing alterations, hypotonia, epilepsy, and cerebral atrophy. The onset of regression is variable. Typically males are affected with MHBD deficiency, however, carrier females can present with a milder phenotype. Females can have mild to moderate developmental delay but do not show regression. Garcia-Willoria et al. found HSD17B10 mutations in affected individuals in two families.

For patients with suspected HSD17B10-related disorder, 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:

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OMIM #300256: HSD17B10 gene
OMIM #300220: XLMR 10
OMIM #300705: XLMR 17
OMIM #300438: MHBD

Genes

HSD17B10

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of HSD17B10-Related Disorder in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of HSD17B10-Related Disorder 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) 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 HSD17B10 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.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90 genes.