X-linked Intellectual Disability: Deletion/Duplication Panel

Test Code: DXLI1  
Turnaround time: 2 weeks  
CPT Codes: 81161 x1, 81244 x1, 81304 x1, 81403 x1, 81404 x1, 81405 x1

Condition Description

Intelectual 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 a syndrome, and carrier females can also be affected, but typically have milder clinical symptoms.

A majority of individuals with XLID are non-syndromic with no other features to assist in diagnosis. Because of the number of genes involved, it is very difficult to identify which X-linked gene may be responsible for the phenotype in any given patient. Simultaneous testing of all known XLID genes in a single study provides a significant diagnostic advantage over single gene sequencing. Additional benefits for the patient and families include:

- Providing information for recurrence risk and family planning and allowing for presymptomatic support
- Helping physicians determine appropriate follow-up testing and develop a health maintenance plan
- Predicting better patient prognostic value
- Assisting researchers in the understanding of the molecular basis of disease in the hope for treatments and cures
- Assessing the possibility of therapy for some forms of XLID

Testing for fragile X syndrome and genomic array CGH testing are recommended as first steps for individuals who may have XLID. If those tests results are normal, XLID gene sequencing panels can be ordered.

Genes

ACSL4, AFF2, AP1S2, ARHGEF8, ARX, ATP6AP2, ATP7A, ATRX, BCO2, BRWD3, CASK, CCDC22, CDK16, CDKL5, CLIC2, CNKSR2, CUL4B, DCX, DKK1, DLG3, DMD, FANC8, FGZ1, FLNA, FM11, FMR1, FPRP2, FTSJ1, GDI1, GKR, GPC3, GRIA3, HCCS, HCCF1, HPRT1, HSD17B10, HUWE1, IES, IGBP1, IL1RAP1, IQSEC2, KDM5C, KIAA0222, KLF4, L1CAM, L4M2, MAOA, MBTPS2, MECP2, MED12, MID1, NAA10, NDE, NDUFA1, NHS, NLGN3, NLGN4X, NSDHL, OCRL, ODF1, OPN1, OTO, PAK9, PCH13, PDHA1, PGK1, PHF6, PHF8, PLP1, PORCN, POBP1, PRPS1, PTCHD1, RAB39B, RBM10, RPL10, RPS6KA3, SHROOM4, SLC16A2, SLC9A6, SMC1A, SMS, SOX3, SYN1, SYP, TIMM8A, TSPAN7, UBE2A, UFSP3B, ZDHHC15, ZDHHC9, ZNF711

Indications

This test is indicated for:

- Individuals with a clinical and family history consistent with an X-linked intellectual disability disorder after fragile X testing and genomic array testing are normal.
- Carrier testing in adult females with a family history of X-linked intellectual disability.

Methodology

Deletion/Duplication Analysis: DNA isolated from peripheral blood is hybridized to a gene-targeted CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes that 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

Deletion/Duplication Analysis: 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

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: Ship sample at room temperature with overnight delivery.

Type: Isolated DNA

Specimen Requirements:

In microtainer: 10 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

Related Tests

- The Autism Panel is available to detect the most common known genetic causes of autism/ID. The autism panel includes testing for fragile X syndrome and chromosome microarray analysis (using oligonucleotide array) and is recommended before XLID gene sequencing panel testing.
- Testing is also available for individual XLID genes that have specific phenotypes.
- 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.
- X-linked Intellectual Disability: Sequencing Panel.