In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic elements mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Testing includes trinucleotide repeat analysis for the *FMR1* (test code: MFRA) gene.

### Genes

- *ACSL4*, *AFF2*, *AP1S2*, *ARHGEF8*, *ARX*, *ATP6AP2*, *ATP7A*, *ATRX*, *BCCOR*, *BRWD3*, *CASK*, *CCDC22*, *CDK16*, *CDKL5*, *CLIC2*, *CNKSR2*, *CUL4B*, *DCX*, *DKC1*, *DLC3*, *DMD*, *FANCB*, *FGD1*, *FLNA*, *FMR1*, *FRMPD4*, *FTSJ1*, *GDI1*, *GKC3*, *GRIK3*, *HCC5*, *HCFC1*, *HPRT1*, *HSD17B10*, *HUC1*, *IDS*, *IGBP1*, *IL1RAPL1*, *IQSEC2*, *KDM3C*, *KLF8*, *L1CAM*, *LAMP2*, *MAOA*, *MBTPS2*, *MECP2*, *MED12*, *MID1*, *NAA10*, *NDP*, *NDFU1*, *NEXMIF*, *NHS*, *NLGN3*, *NLGN4X*, *NSDHL*, *OCRL*, *OFD1*, *OPHN1*, *OTC*, *PARK*, *PCDHN1*, *PDGFR*, *PHEF*, *PHF8*, *PLP1*, *PORCN*, *PQBP1*, *PRPS1*, *PTCHD1*, *RAB3B*, *RB1*, *RPL10*, *RPS6KA3*, *SHROOM4*, *SLC16A2*, *SLC9A6*, *SMC1A*, *SMS*, *SOX3*, *SYN1*, *SYNGAP1*, *SYP*, *TIMM8A*, *TSPAN7*, *UBE2A*, *UF2F*, *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

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### Detection

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%

**MFRA:**

- Normal: Approximately 5-44 CGG repeats.
- Intermediate: Approximately 54-45 unmethylated CGG repeats.
- Premutation: Approximately 55-200 CGG repeats and methylation of expanded allele.
- Affected: Over 200 CGG repeats and methylation of expanded allele.

### Reference Range

**Next Generation Sequencing:** N/A.

**FRAX:**
Normal: Approximately 5-44 CGG repeats.
Intermediate: Approximately 54-45 unmethylated CGG repeats.
Premutation: Approximately 55-200 CGG repeats and methylation of expanded allele.
Affected: Over 200 CGG repeats and methylation of expanded allele.

**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: Isolated DNA**

Specimen Requirements:

- In microtainer: 60 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: Deletion/Duplication Panel.