Autism Spectrum Disorders Tier 2 Panel: Sequencing and CNV Analysis

Test Code: MM021
Turnaround time: 6 weeks
CPT Codes: 81243 x1, 81302 x1, 81321 x1, 81401 x1, 81404 x1, 81405 x1, 81406 x1, 81407 x1, 81408 x1

Condition Description

Genetics of Autism Spectrum Disorders
Autism spectrum disorders (ASDs) are a group of neurodevelopmental disorders which include autism, pervasive developmental delay—not otherwise specified (PDD-NOS), and Asperger syndrome. ASDs are characterized by impairments in social relationships, variable degrees of language and communication deficits, and repetitive behaviors and/or a narrow range of interests. The age of onset is prior to age 3 with a variable clinical presentation, ranging in severity both amongst individuals as well as amongst the various subtypes of ASDs. Additional clinical features may also be observed in individuals with an ASD, such as intellectual disability (up to ~50%) and seizures (~25%).

Known genetic causes of autism include cytogenetically visible chromosome abnormalities (3-5%), copy number variants – which include submicroscopic deletions and duplications (~6-7%), and single gene disorders (~5%).

EGL Genetics’s integrated testing strategy allows for a comprehensive cytogenetics, metabolic, and molecular analysis of ASD in your patient. For a summary of autism testing at EGL, please click here.

*Please note that some genes on this panel are associated with additional phenotypes.

All components of the Autism Panel can be ordered separately.

References:


Genes

ADSL, AFF2, ALDH5A1, AP1S2, ARX, ATRX, BCKDK, BRAF, CACNA1C, CASK, CDKL5, CHD7, CHD8, CNTNAP2, CREBBP, CYP27A1, DHCR7, DMD, EHMT1, FGD1, FMR1, FOLR1, FOX1, FOXP1, FOXP2, HPRT1, KDM5C, L1CAM, MAGEL2, MBD5, MECP2, MED12, MEF2C, MID1, NHS, NIPBL, NLGN3, NLGN4X, NR1I3, NRXN1, NSD1, OPHN1, PAFH1B1, PCDH19, PHF6, PNKP, POBP1, PTCHD1, PTK2, PTEN, PTPN11, RAB39B, RA1, RELN, SCN1A, SLC2A1, SLC9A6, SMARCB1, SMCP1A, TCF4, UBE2A, VPS13B, ZEB2

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of autism or an autism spectrum disorder.
- Carrier testing in adults with a family history of autism or an autism spectrum disorder.

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.

Copy Number Analysis: Comparative analysis of the NGS read depth (coverage) of the targeted regions of genes on this panel was performed to detect copy number variants (CNV). The accuracy of the detected variants is highly dependent on the size of the event, the sequence context and the coverage obtained for the targeted region. Due to these variables and limitations a minimum validated CNV size cannot be determined; however, single exon deletions and duplications are expected to be below the detection limit of this analysis.

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. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical sensitivity for sequence variant detection is ~99%.
Copy Number Analysis: The sensitivity and specificity of this method for CNV detection is highly dependent on the size of the event, sequence context and depth of coverage for the region involved. The assay is highly sensitive for CNVs of 500 base pairs or larger and those containing at least 3 exons. Smaller (< 500 base pairs) CNVs and those that involving only 1 or 2 exons may or may not be detected depending on the sequence context, size of exon(s) involved and depth of coverage.

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<th>Reference Range</th>
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Next Generation Sequencing: NA

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<th>Specimen Requirements</th>
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Submit only 1 of the following specimen types

**Type: Whole Blood (EDTA)**

Specimen Requirements:
EDTA (Purple Top)
Infants and Young Children (2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

**Type: DNA, Isolated**

Specimen Requirements:
Microtainer
20µg
Isolation using the Perkin Elmer™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

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

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<th>Related Tests</th>
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- Autism Spectrum Disorders Panel: Complete Tier 1
- Autism Spectrum Disorders Panel: Tier 1 Cytogenetics and Molecular
- Autism Spectrum Disorders Panel: Tier 1 Biochemical
- Autism Spectrum Disorders: Deletion/Duplication Analysis