

Autism Spectrum Disorders: Complete Tier 1 Panel

Test Code: XC020

Turnaround time: 3 weeks

CPT Codes: 82139 x1, 81228 x1, 81243 x1, 82542 x1, 82570 x1, 83789 x1, 83864 x1, 83918 x1, 84375 x1, 84377 x1, 88230 x1

Condition Description

Notice: This test will soon be discontinued.

As of 02/01/2020, EGL can no longer accept samples for this test. For questions, please call: 470-378-2200.

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 cytogenetic, metabolic, and molecular analysis of ASD in your patient. For a summary of autism testing at EGL, please click [here](#).

* Please note that Tier 1 testing may be ordered as a complete panel [Autism Panel – Complete Tier 1] or individually [Tier 1 - Cytogenetics and Molecular Only or Tier 1 - Biochemical Only].

References:

- Autism and Developmental Disabilities Monitoring Network Surveillance Year 2006 Principal Investigators and the CDC (2009). *MMWR Surveill Summ*, 58:1-20.
- Bolton *et al.* (2011). *Br J Psychiatry*, 198:289-294.
- Vorstman *et al.* (2006) *Mol Psych*, 11:18-28.
- Shen *et al.* (2010). *Pediatrics*, 125:e727-35.
- Miles JH (2011). *Genet Med*, 13:278-94.
- Schaefer *et al.* (2008). *Genet Med*, 10:301-5.

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

EmArray Cyto: DNA isolated from peripheral blood is hybridized to a custom array containing oligonucleotide probes across the genome to detect copy number imbalances. FISH analysis or another method, such as G-banding, is used to confirm any abnormal findings either at the time of initial testing or upon receipt of parental samples, depending on the abnormality.

Fragile X: Both normal CGG repeat tracts and expanded CGG repeat tracts are detected by PCR amplification, using a CGG repeat-specific probe, and capillary electrophoresis. Expanded CGG repeat tracts will be reflexed to a gene specific PCR and sized by agarose gel electrophoresis. DNA methylation analysis will be performed on any full expansions detected, Methylation sensitive PCR for Males and Southern blot for females.

Urine Organic Acids: Qualitative and quantitative determination performed by gas chromatography/mass spectrometry.

Plasma amino acids: Quantitative ion exchange chromatography, reported as micromoles/L creatinine.

Smith-Lemli-Opitz Screen: Isotope dilution method by LC-MSMS

Oligosaccharides: The traditional one-dimensional thin-layer chromatography method for urine oligosaccharides analysis has limited specificity and sensitivity and provides no structural information that is often needed for diagnoses. This test provides a sensitive screening method for structural analysis of urinary oligosaccharides, glycan and glycoamino acids by liquid chromatography-mass spectrometry using quadrupole - time of flight detection.

GAGS: Dimethylene Blue Binding Quantitation and Thin Layer Chromatography

Detection

EmArray Cyto: The detection of deletions and duplications of 500 kb or greater is expected to be very high. Detection is limited to gain of copy number (duplication), loss of copy number (deletion) or normal copy number. Deletions and duplications of 500 kb or greater are reported. Smaller deletions or duplications in regions of known microdeletion/microduplication syndromes or in clinically relevant genes will also be reported. The clinical sensitivity for known microdeletion or microduplication syndromes is available in our detection rate chart. The clinical sensitivity for other disorders is dependent on the proportion of cases caused by deletions/duplications compared with other mutations not detectable by array analysis. Microarray will not detect balanced translocations, balanced inversions, imbalances smaller than the resolution of this array, point mutations or low level mosaicism (usually less than 25%) that may underlie the clinical presentation of the patient.

Fragile X: All cases of fragile X syndrome caused by CGG expansion will be detected by this assay. Rare cases of fragile X syndrome caused by mutation of the FMR1 gene will not be detected by this assay.

10-15% of patients with autism are diagnosed with an identifiable chromosomal rearrangement or fragile X syndrome, using the above methodologies.

Urine Organic Acids: Test results can be influenced by the age and eating status of the patient. A second test (amino acids analysis/acylcarnitine profile) is typically required to confirm a diagnosis.

Plasma Amino Acids: This test is very sensitive for specific amino acid disorders, but detection can be sensitive to the age and eating status of the patient.

Smith-Lemli-Opitz Screen: Mild elevations of 7-dehydrocholesterol can occur in patients with hypercholesterolemia and those receiving treatment with haloperidol. Only patients with Smith-Lemli-Opitz syndrome have elevated 7-dehydrocholesterol/cholesterol ratios.

Lysosomal Storage Disease Screen: This test provides a comprehensive tool for initial screening of lysosomal storage disorders. The combination of urine oligosaccharide/free glycan and urine quantitative and fractionation of GAG's increases the sensitivity and specificity of urinary screening for lysosomal storage disorders. Due to the increased sensitivity of the mass spectrometry method, the urine oligo/free glycan profiles can detect lysosomal dysfunctions due to the accumulation of charged storage material such as glycosaminoglycans. While the quantification and fractionation of glycosaminoglycans provides additional information that differentiates between the different types of mucopolysaccharidosis. Abnormal results should be confirmed by enzyme and molecular analysis.

Reference Range

EmArray Cyto: Ratio of 1.2 for duplication.

Fragile X: 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.

Urine Organic Acids: Will be included with report

Plasma Amino Acids: Will be included with report

Smith-Lemli-Opitz Screen: Reporting will be normal or abnormal based on the value of 7-dehydrocholesterol

Lysosomal Storage Disease Screen: Interpretation of the urinary oligosaccharide and free glycan profiles is by pattern recognition.

Specimen Requirements

Submit all 3 of the following specimens

Type: Urine

Specimen Requirements:

Clean container without additives

15-30 ml

Freeze sample. Fasting or first void sample is preferable.

Specimen Collection and Shipping:

Ship frozen sample on dry ice with overnight delivery.

Type: Whole Blood (EDTA and Sodium Heparin)

Specimen Requirements:

Sodium Heparin and EDTA

Infants (Children (>2 years): 3-5 ml in both tubes

Older Children & Adults: 7-10 ml in both tubes

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

Related Tests

- Autism Panel: Tier 1 Cytogenetic and Molecular
- Autism Panel: Tier 1 Biochemical
- Autism Panel: Tier 2