Autism Spectrum Disorders: Complete Tier 1 Panel

**Test Code:** XC020  
**Turnaround time:** 3 weeks  
**CPT Codes:** 81228 x1, 81243 x1, 82139 x1, 82542 x1, 82570 x1, 83789 x1, 83864 x1, 83918 x1, 84375 x1, 84377 x1, 88230 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 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:


### 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:** Isootope dilution method by LC-MSMS

**Oligosaccharides:** MALDI-TOF/TOF. 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 diagnosis. This test provides a sensitive screening method for structural analysis of urinary oligosaccharides, glycan and glycoamino acids by Matrix-Assisted Laser Desorption/Ionization-Time of flight/Time of flight (MALDI-TOF/TOF).

**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 extreme sensitivity of the MALDI-TOF/TOF 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 mucopolysaccharidoses. 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: Click here for reference range.

Plasma Amino Acids: NA

Smith-Lemli-Opitz Screen: Reporting will be normal or abnormal based on the value of 7-dehydrocholesterol and the ratio of 7-dehydrocholesterol/cholesterol.

Normal ranges:

- 7-dehydrocholesterol (plasma) <2.67 ug/ml
- Cholesterol (plasma) <2098 ug/ml
- Ratio of 7-dehydrocholesterol/cholesterol 0.003

Lysosomal Storage Disease Screen: Interpretation of the urinary oligosaccharide and free glycan profiles is by pattern recognition. And link to reference ranges

Specimen Requirements

Additional Specimen Collection/Handling Instructions Required for this Test
Due to the different shipping and handling instructions for the three specimen types, the plasma and urine should be shipped in a separate container from the whole blood.

Submit all 3 of the following specimens

Type: Whole Blood
Specimen Requirements:

In EDTA (purple top) AND sodium heparin (green top) tubes:
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.

Type: Plasma
Specimen Requirements:
In sodium heparin (green top) tube: 2-5 ml

Sample should be collected while fasting or 2-4 hours postprandial.

Centrifuge to separate plasma and freeze.

Specimen Collection and Shipping: Ship frozen sample on dry ice with overnight delivery.

**Type: Urine**

Specimen Requirements:

In a clean container without preservatives: 15-30 ml. Freeze.

Fasting or first void sample is preferable.

Specimen Collection and Shipping: Ship frozen sample on dry ice with overnight delivery.

**Related Tests**

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