Autism Spectrum Disorders: Tier 1 Cytogenetic and Molecular Panel

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%).

Emory Genetics Laboratory’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.

All components of the Autism Panel can be ordered separately.

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.

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/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.

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

### Specimen Requirements

#### Additional Specimen Collection/Handling Instructions Required for this Test
Both tube types are required for this test. Testing cannot be initiated until both tubes are received.

#### 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.

### Related Tests

- Autism Panel: Complete Tier 1
- Autism Panel: Tier 1 Biochemical
- Autism Panel: Tier 2