Autism and Intellectual Disability Comprehensive Panel

**Background**

Autism spectrum disorders (ASDs) and intellectual disability (ID) represent a neurodevelopmental continuum with significant comorbidity and overlapping etiology.

ASD is classified by varying degrees of social impairment, communication, repetitive behaviors, and/or restricted interests. Symptoms typically present by age 3 and medical diagnoses are made clinically based on severity of symptoms.

Comorbidities often include but are not limited to ID, attention deficit hyperactivity disorder (ADHD), epilepsy, language deficits, and gastrointestinal issues. Likewise, ID shares comorbidities with ASD and is classified by broad impairment in cognitive and adaptive development with an IQ below 70 diagnosed before age 18.

ASDs and/or ID may be a feature in various genetic syndromes associated with chromosomal copy number variants (CNVs), fragile X syndrome, and inborn errors of metabolism (IEMs). Literature suggests ~10-15% of individuals with ASD and/or ID have detectable chromosomal abnormalities associated with CNVs and fragile X syndrome, while up to 5% of ASD and up to 8% of ID may be related to potentially treatable IEMs.

**Heritability**

- ASD – ~90%
- ID – ~50%

**Incidence**

- ASD – ~1/68 (1/42 males, 1/189 females)
- ID – ~1/100
- ASD and ID combined incidence – ~1/250

**Indications for Ordering**

- Comprehensive evaluation of an individual with ASD and/or ID/developmental delay (with or without comorbidities)
- Assist with decisions about treatment and management of an individual with ASD or ID
- Confirmation of a clinical diagnosis of ASD and/or ID

**Tests to Consider**

**Primary test**

**Autism and Intellectual Disability Comprehensive Panel 2014314**

- Comprehensive genetic evaluation of individuals with ASD and/or ID
- Includes cytogenomic microarray, fragile X methylation analysis, and comprehensive metabolic disorders analysis

**Test components**

**Cytogenomic SNP Microarray 2003414**

- May be ordered separately as first-tier test for developmental delay, multiple anomalies, ID, and ASD
- Affymetrix CytoScan HD platform to detect CNV changes such as microdeletions and duplications and long contiguous stretches of homozygosity

**Fragile X (FMR1) with Reflex to Methylation Analysis 2009033**

- May be ordered separately as preferred test to diagnose fragile X syndrome and for carrier screening in individuals with positive family history
- If fragile X testing detects a CGG repeat of 55 or greater by polymerase chain reaction and capillary electrophoresis, methylation analysis will be added

**Autism and Intellectual Disability Metabolic Panel 2014312**

- May be ordered separately for evaluation of ASD and/or ID in individuals who have had negative FMR1 (fragile X) and cytogenomic SNP microarray testing
- **Acylcarnitine Quantitative Profile, Plasma 0040033**
  - Quantitative tandem mass spectrometry
- **Amino Acids Quantitative by LC-MS/MS, Plasma 2009389**
  - Quantitative liquid chromatography/tandem mass spectrometry
- **Creatine Disorders Panel, Serum or Plasma 2002328**
  - AND
- **Creatine Disorders Panel, Urine 2002333**
  - Order these two tests simultaneously for proper result interpretation
  - Liquid chromatography/tandem mass spectrometry
- **Mucopolysaccharides Screen, Urine 0081352**
  - Spectrophotometry and electrophoresis
- **Organic Acids, Urine 0098389**
  - Gas chromatography/mass spectrometry

**Confirmation of a clinical diagnosis of ASD and/or ID**
Test Limitations

- Autism panel testing limitations
  - Other etiologies of ASD and ID, such as single gene disorders, may not be identified
  - Uninformative results may occur due to variants of uncertain clinical significance
  - Results may not predict disorder severity
- Cytogenomic SNP microarray does not detect
  - Base-pair mutations
  - Very small deletions/duplications
  - Balanced rearrangements (translocations, inversions, balanced insertions)
  - Imbalances of the mitochondrial genome
  - Low-level mosaicism (<25%)
  - For further review, see Additional Technical Information for Cytogenomic SNP Microarray 2003414
- Fragile X testing limitations
  - Estimated size is not provided for full mutations with >200 repeats
  - Rare mutations in FMR1 unrelated to trinucleotide expansion will not be detected
  - Diagnostic errors can occur due to rare sequence variations
  - For further review, see Additional Technical Information for Fragile X (FMR1) with Reflex to Methylation Analysis 2009033

References