**Condition Description**

Mutations in the *NLGN3* (Xq13) and *NLGN4X* (Xq22.33 – also referred to as *NLGN4*) genes have been found in less than 1% of individuals with autism spectrum disorder (ASD). The clinical phenotype of affected individuals varies widely and can include autism of variable severity, X-linked intellectual disability without autism, Asperger syndrome, and pervasive developmental delay not otherwise specified (PDD-NOS). Onset may be gradual or abrupt and regression of milestones may occur. There are usually no dysmorphic features present. Carrier females are often unaffected, but neuropsychiatric disorders have been reported in a female carrying a deletion of exons 4-6 of *NLGN4X*.

For patients with suspected *NLGN4X*-Related X-Linked Susceptibility to Autism Spectrum Disorder, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

This testing is for mutation in the *NLGN4X* gene only.

**References:**

- GeneReviews
- OMIM #300427: *NLGN4X* gene
- OMIM #300495: X-Linked Autism Disorder
- OMIM #300497: X-Linked Asperger Syndrome

**Genes**

*NLGN4X*

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of *NLGN4X*-Related X-Linked Susceptibility to Autism Spectrum Disorder in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of *NLGN4X*-Related X-Linked Susceptibility to Autism Spectrum Disorder in whom sequence analysis was negative.

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types
* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

### Related Tests

- Sequence analysis of the *NLGN4X* gene is available and is required before deletion/duplication analysis.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90 genes.
- Sequencing and deletion/duplication analysis are also available for the *NLGN3* gene.