ARX-related Disorders: ARX Gene Deletion/Duplication

Test Code: RW  
Turnaround time: 2 weeks  
CPT Codes: 81403 x1

Condition Description

Mutations of the ARX gene have recently been identified as contributors to X-linked intellectual disability (XLID), both syndromic and non-syndromic. The phenotypic expression varies, and mutations in ARX have been associated with syndromic conditions such as:

- West syndrome
- Partington syndrome
- X-linked lissencephaly with abnormal genitalia (XLAG)
- Ohtahara syndrome
- Proud syndrome.

The West syndrome phenotype includes infantile spasms, hypsarrhythmia, and intellectual disability.

Partington syndrome characteristics include intellectual disability with dystonic movements, ataxia, and seizures.

Ohtahara syndrome includes early infantile epileptic encephalopathy with suppression-burst pattern.

The Proud syndrome phenotype is composed of intellectual disability with agenesis of the corpus callosum, microcephaly, limb contractures, scoliosis, coarse facies, tapered digits, and urogenital abnormalities. Female carriers are not clinically affected.

The ARX gene maps to Xp22.13 and belongs to the family of aristaless-related paired-class homeobox genes. These genes are transcription factors and function as key players in vertebrate embryology. The ARX protein is a crucial gene for the development of interneurons in the fetal brain.

Mutations identified in ARX have included:

- Polyalanine repeat tract expansions
- Missense mutations
- Nonsense mutations
- Premature termination mutations
- Frameshift mutations
- Splice site mutations
- Duplications/insertions, and large deletions.

For patients with a suspected ARX-related 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.

Please click here for the OMIM summary on this condition.

Genes

ARX

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of an ARX-related disorder in an individual in whom sequencing analysis was negative.
- Carrier testing in adult females with a family history of an ARX-related disorder in whom sequencing 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

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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\textsuperscript{TM} 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.

**Special Instructions**

Please submit copies of diagnostic biochemical test results along with the sample, if appropriate. Contact the laboratory if further information is needed. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- ARX Gene Sequencing (RV) is required before deletion/duplication analysis.

Prenatal Custom Diagnostics is available to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.