EGL Genetics | Eurofins Clinical Diagnostics
2460 Mountain Industrial Boulevard | Tucker, Georgia 30084
Phone: 470-378-2200 or 855-831-7447 | Fax: 470-378-2250
eglgenetics.com

ARX-related Disorders: *ARX* Gene Sequencing

Test Code: RV
Turnaround time: 4 weeks
CPT Codes: 81404 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 such syndromic conditions as West syndrome, Partington syndrome, X-linked lissencephaly with abnormal genitalia (XLAG), Ohtahara syndrome, and 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.

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
- Carrier testing in adult females with a family history of an *ARX*-related disorder

Methodology

Full Gene Sequencing: PCR amplification of 5 exons contained in the *ARX* gene is performed on patient genomic DNA. Direct sequencing of amplification products is performed in both the forward and reverse directions using automated fluorescence dideoxy sequencing methods. Patient gene sequences are compared to a normal reference sequence. Sequence variations are then classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions or other regulatory elements. Large deletions are not detected by this analysis.

Detection

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:
Microtainer
8µg
Isolation using the Perkin Elmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Whole Blood (EDTA)

Specimen Requirements:

2460 Mountain Industrial Boulevard | Tucker, Georgia 30084
Phone: 470-378-2200 or 855-831-7447 | Fax: 470-378-2250
eglgenetics.com

EDTA (Purple Top)
Infants and Young Children (2 years of age to 10 years old: 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Orangene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Special Instructions

Submit copies of diagnostic biochemical test results 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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

Related Tests

- Deletion/duplication analysis of the *ARX* gene by CGH array is available for those individuals in whom sequence analysis is negative (RW).
- A CGH array-based test for deletion/duplication analysis of 64 different X-linked intellectual disability genes is available (OL).
- 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 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.