X-Linked Adrenoleukodystrophy Testing

X-linked adrenoleukodystrophy (X-ALD) is a rare X-linked metabolic disorder caused by variants in the *ABCD1* gene that cause a deficiency in adrenoleukodystrophy protein (ALDP) and subsequent accumulation of very long-chain fatty acids (VLCFAs). VLCFA accumulation occurs in plasma and all tissue types, but primarily affects the adrenal cortex and white matter of the brain and spinal cord, resulting in a range of clinical outcomes.

Adrenal insufficiency may be the initial presentation of X-ALD, and 21-hydroxylase antibody testing may confirm or exclude an autoimmune etiology. In X-ALD, 21-hydroxylase antibody testing results will be normal; therefore, males with adrenal insufficiency and normal 21-hydroxylase antibody testing should be tested for X-ALD (VLCFA profile).

Testing Strategy

**Diagnostic Testing**

- VLCFA and branched-chain fatty acid (BCFA) profile is the first-line test for an individual with suspected X-ALD or adrenomyeloneuropathy
- Molecular testing (*ABCD1*) is recommended for diagnostic confirmation in individuals with clinical and/or biochemical presentation of X-ALD

**Disease Overview**

**Incidence**

1/14,700 live births

**Genetics**

**Gene**

*ABCD1*

**Structure**

*ABCD1* gene, contains 10 exons

**Inheritance**

X-linked

**Penetrance**

Neurologic symptoms are present in nearly 100% of males by adulthood.

**Variants**

- Most are specific to a particular family (“private variants”)
- ~4-19% of individuals with X-ALD have a de novo variant

Tests to Consider

See Testing Strategy

**Very Long-Chain and Branched-Chain Fatty Acids Profile 2004250**

**Method:** Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

- Biochemical test to measure concentration of very long-chain fatty acids (VLCFAs) C22-C26, pristanic acid, and phytanic acid
- Initial test to screen for disorders of peroxisomal biogenesis and/or function, including X-ALD and Zellweger syndrome
- Confirmatory test for abnormal newborn screening suggestive of X-ALD

**Familial Targeted Sequencing 3005867**

**Method:** Massively Parallel Sequencing

- Testing for a known familial sequence variant by sequencing gene of interest. A copy of the family member’s test result documenting the familial gene variant is REQUIRED.
- To determine if the variant(s) of interest are detectable by this assay, contact an ARUP genetic counselor at 800-242-2787.
For more information on the disease including testing strategy, disease overview, and genetics, visit the X-Linked Adrenoleukodystrophy topic in ARUP Consult.

Test Interpretation

Biochemical testing (VLCFAs and BCFAs)

- Elevated VLCFAs in males
- ~85% of heterozygous female carriers will have elevated VLCFAs

References


Additional Resources


Related Information

X-Linked Adrenoleukodystrophy