

Alström Syndrome via *ALMS1* Gene Sequencing (Test #265)

Brief Description of Clinical Features: Alström syndrome (ALMS or ALSS; OMIM 203800) is a pleiotropic disorder characterized by retinal degeneration, childhood obesity, sensorineuronal hearing loss, diabetes Mellitus, dilated cardiomyopathy and urological, renal, hepatic and pulmonary dysfunctions (Collin et al. Nat Genet 31:74-78, 2002; Marshall et al. Hum Mutat 28:1114-1123, 2007).

Although Alström syndrome bears many similarities to the Bardet-Biedl syndrome (OMIM 209900), there is no cognitive impairment, polydactyly, or hypogonadism (Alström et al. Acta Psychiatr Neurol Scand Suppl 129:1-35, 1959; Marshall et al. 2007). The retinal lesion, nystagmus and early loss of central vision usually present in Alström syndrome overlap with the clinical findings in Achromatopsia (OMIM 262300, 216900 and 613093) and Leber congenital amaurosis (OMIM 204000 and 204100) (Marshall et al. 2007; Russell-Eggitt et al. Br J Ophthalmol 73:250-254, 1989).

Genetics: Alström syndrome is inherited as an autosomal recessive disorder (Alström et al. 1959; Goldstein and Fialkow. Medicine 52: 53-71, 1973), and is caused by mutations in the *ALMS1* gene (Collin et al. 2002). *ALMS1* encodes Alström syndrome protein 1, which is localized to centrosomes and basal bodies of ciliated cells (Marshall et al. 2007). Although, the precise function of *ALMS1* protein is unknown, the localization of the *ALMS1* protein suggests a role in intracellular trafficking and cilia function (Collin et al. 2002; Hearn et al. Diabetes 54:1581-1587, 2005). A mix of missense, nonsense, frameshift and splicing mutations as well as gross deletions have been reported in *ALMS1* (Collin et al. 2002; Hearn et al. Nat Genet 31:79-83, 2002; Marshall et al. 2007; Aldahmesh et al. Am J Med Genet 149A(4):662-665, 2009; Bond et al. J Med Genet J 42:e10, 2005).

Description of This Particular Test: This test involves bidirectional sequencing using genomic DNA of all the 23 coding exons (exon 1-23) of the *ALMS1* gene plus ~50 bp of flanking non-coding DNA on each side. The test starts with sequencing of exons 8, 10 and 16. If no causative mutation or only one mutation is found, then we proceed with sequencing the remaining 20 exons. As indicated, we will also perform sequencing of any single exon (Test # 100) or pair (Test # 200) of exons for family members of patients with known mutations and to confirm previous research results (\$190-340 charge).

Reference Sequences: Genomic: NC_000002.11 mRNA: NM_015120.4 Protein: NP_055935.4 (CCDS42697.1)

Indications for Test: Candidates for this test are patients with symptoms consistent with Alström syndrome and family members of patients who have known *ALMS1* mutations.

Sensitivity of Test: Sensitivity of this test is currently unknown. However, DNA sequencing analysis of exons 16, 10 and 8 is expected to detect 25% – 40% of the *ALMS1* mutations (Marshall et al. 2007).

Turnaround Time: Maximum of 40 calendar days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See page 4 of the Requisition Form.

Prices: Sequencing of exons 8, 10 and 16 of the *ALMS1* gene **\$1,090**
 Sequencing of the full *ALMS1* gene **\$1,990**

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x43	83898 \$ 660	Sequencing x43	83904 \$ 990
Separation x1	83894 \$ 140	Interpretation/Report x1	83912 \$ 130

Accreditation: CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

Contact: Dr. Keith Nykamp, keith.nykamp@preventiongenetics.com, www.preventiongenetics.com