

## Juvenile Amyotrophic Lateral Sclerosis, Autosomal Recessive via *ALS2* Gene Sequencing (Test #108)

**Brief Description of Clinical Features:** Amyotrophic lateral sclerosis (ALS, OMIM 105400) is a neurodegenerative disease characterized by selective loss and dysfunction of both upper motor neurons (UMN) of the motor cortex and lower motor neurons (LMN) of the brainstem and spinal cord (Tandan and Bradley Ann Neurol 18:271-280, 1985; Brooks, J Neurol Sc, 124 (Sup):96-107, 1994). The dysfunction and loss of UMN result in spasticity in the legs leading to difficulty in walking, lack of movement coordination and brisk reflexes. Damage to LMN results in weakness, muscle wasting and fasciculation. Symptoms usually begin with asymmetric involvement of the muscles. Juvenile ALS (ALSJ, ALS2, AR-ALS OMIM 205100) is distinguished from the classical ALS by its early onset and slow progression. In ALSJ, the age of onset varies between 3 and 10 years of age and the mean disease duration ranges between 2 and 28 years (Ben Hamida et al. Brain 113 (Pt 2): 347-363, 1990). As is the case for classical ALS, ALSJ is clinically heterogeneous, and its phenotype is influenced by the relative ratio of UMN and LMN involvement (Yang et al. Nat Genet 29: 160-165, 2001).

**Genetics:** ALSJ is most often inherited with an autosomal recessive pattern, and has been generally reported in North African (Hentati et al. Nat Genet 7: 425-428, 1994) and Middle Eastern populations (Kress et al. Ann Neurol 58: 800-803, 2005). ALSJ is caused by mutations in the *ALS2* gene (Yang et al. Nat Genet 29: 160-165, 2001; Hadano et al. Nat Genet 29: 166-173, 2001; Kress et al. Ann Neurol 58: 800-803, 2005; Bertini et al. GeneReviews, www.genetests.org, 2005). To date, three small homozygous deletions were reported in patients with ALSJ from consanguineous families. All deletions resulted in a predicted truncated protein with loss of function. In addition to ALSJ, mutations in the *ALS2* gene were reported in patients with juvenile primary lateral sclerosis (PLSJ, OMIM 606353), infantile-onset ascending spastic paralysis (IAHSP, OMIM 607225) and complicated hereditary spastic paraplegia (cHSP, Gros-Louis et al. Ann Neurol 53: 144-145, 2003).

**Description of This Particular Test:** The *ALS2* gene encodes the Alsin protein. This test involves bidirectional DNA sequencing of all 33 coding exons and splice sites of the *ALS2* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. We will sequence any single exon or pair of exons in family members of patients with known mutations and to confirm results.

**Reference Sequences:** Genomic: **NC\_000002.10** mRNA and protein: **CCDS 42800.1**

**Indications for Test:** All patients with symptoms suggestive of ALSJ as described above. The *ALS2* gene is also a candidate for patients with PLSJ (OMIM, 606353), IAHSP (OMIM, 607225) and cHSP (Gros-Louis et al. Ann Neurol 53:144-145, 2003).

**Sensitivity of Test:** Currently unknown.

**Turn Around Time:** Maximum of 40 calendar days.

**Specimen Requirements:** See page 4 of Requisition Form.

**Price:** **Sequencing of all coding exons of the *ALS2* Gene:** **\$ 1790**

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x 37	83898 \$ 610	Sequencing x 37	83904 \$ 910
Separation x1	83894 \$ 90	Interpretation/Report x1	83912 \$ 110

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

**Contact for info:** Dr. Khemissa Bejaoui, [khemissa@preventiongenetics.com](mailto:khemissa@preventiongenetics.com), [www.preventiongenetics.com](http://www.preventiongenetics.com)