

Amyotrophic Lateral Sclerosis / Motor Neuron Disease (Autosomal Dominant) via SOD1 Gene Sequencing --Test # 106

Brief Description of Clinical Features: Amyotrophic lateral sclerosis (ALS, OMIM 105400), is a neurodegenerative disease characterized by a selective loss of motor neurons in the motor cortex, brain stem, and spinal cord (Tandan and Bradley, Ann Neurol 18:271-280, 1985). The dysfunction and loss of these neurons result in rapid progressive muscle weakness, atrophy and ultimately paralysis of limb, bulbar and respiratory muscles. The mean age of onset of symptoms is about 55 years of age, however most cases begin between 40 and 70 years of age. The annual incidence of ALS is 1-2 per 100,000 (Cleveland and Rothstein, Nat Rev Neurosci 2(11):806-819, 2001). The most common symptoms include: twitching and cramping of muscles of the hands and feet, loss of motor control in the hands and arms, weakness and fatigue, tripping and falling. Symptoms usually begin with asymmetric involvement of the muscles. As the disease progresses, symptoms may include difficulty in talking, breathing, and swallowing, shortness of breath, and paralysis. See also the Amyotrophic Lateral Sclerosis Fact Sheet (www.ninds.nih.gov/disorders/amyotrophiclateralsclerosis).

Genetics: About 10 % of ALS cases are familial (Emery and Holloway, Adv Neurol 36:139-147, 1982). In most of these families, ALS is inherited with an autosomal dominant (AD-ALS) manner and age-dependant, but high penetrance. In rare families, the disease is transmitted with an autosomal recessive pattern (OMIM 205100). Autosomal recessive ALS is characterized by a juvenile onset and has been mostly reported in North African (Ben Hamida et al., Brain 113:347-363, 1990) and Middle Eastern populations (Yang et al., Nat Genet 29(2):160-165, 2001; Kress et al., Ann Neurol 58(5):800-803, 2005). Autosomal Dominant ALS affects all ethnic groups. This form of the disease is clinically and genetically heterogeneous. At least nine (9) genetic loci have been associated with AD-ALS. To date, four genes have been identified. Mutations in the superoxide dismutase 1 (SOD1) account for about 20 % of AD-ALS cases (Rosen et al., Nature 362:59-62, 1993; Deng et al., Science 261:1047-1051, 1993). Over 120 different SOD1 causative mutations were found. SOD1 mutations are distributed along the entire coding region of the gene. Although most mutations are missense resulting in amino acid substitutions, splice mutations and small deletions or insertions were also reported.

Description of This Particular Test: The *SOD1* gene encodes for superoxide dismutase 1 enzyme, which catalyzes the dismutation of superoxide to hydrogen peroxide and oxygen. This test involves bidirectional DNA sequencing of all 5 coding exons and splice sites of the *SOD1* gene. The full coding sequence of each exon plus ~ 50 bp of flanking-coding DNA on either side are sequenced. We will sequence any single exon in family members of patients with a known mutation.

Reference Sequences: Genomic: **NC_000021.7** mRNA and protein: **CCDS 33536.1**

Indications for Test: All patients with symptoms suggestive of ALS or Motor Neuron Disease, as defined by the El Escorial criteria. See <http://www.wfnals.org/guidelines/1998elescorial/elescorial1998.htm>.

Sensitivity of Test: This test allows the detection of mutations in approximately 20 % of patients with AD-ALS or Motor Neuron Disease (Rosen et al., Nature 362:59-62, 1993).

Turn Around Time: Maximum of 40 calendar days.

Specimen Requirements: See page 4 of the Requisition Form.

Price: **Sequencing of SOD1 Gene Exons 1-5 \$ 490**

CPT Codes:

Sample Ascertainment x1	83890	\$ 30	DNA Isolation x1	83891	\$ 40
Amplification x5	83898	\$ 120	Sequencing x5	83904	\$ 190
Separation x1	83894	\$ 40	Interpretation/Report x1	83912	\$ 70

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, www.preventiongenetics.com