

Tay-Sachs Disease AB Variant/ GM2-Gangliosidosis Variant AB via GM2A Gene Sequencing --Test #478

Brief Description of Clinical Features: Tay-Sachs disease AB Variant, also called GM2-Gangliosidosis variant AB, (OMIM 272750) is the rarest form of GM2-gangliosidoses. This form of the disease is characterized by the accumulation of ganglioside GM2 in brain tissues, similar to classical Tay-Sachs disease with no deficiency of beta-hexosaminidase A activity. Tay-Sachs disease AB Variant is due to defective GM2 activator protein (GM2AP) and is clinically undistinguishable from the classical infantile Tay-Sachs phenotype. Symptoms usually begin in infancy and include psychomotor retardation, motor weakness, hypotonia, hyporeflexia, infantile spasms, motor seizures, myoclonic jerks, exaggerated startle response and impaired sucking and swallowing. Disease progression is rapid and associated with lateral nystagmus, hepatomegaly and brain atrophy (Schepers et al. Am J Hum Genet 59:1048-1056, 1996; Chen et al. Am J Hum Genet 65:77-87, 1999). See also the National Tay-Sachs and Allied Diseases Association at <http://www.ntsad.org/>.

Genetics: Tay-Sachs disease AB Variant is inherited with an autosomal recessive manner and results from mutations in the *GM2A* gene (Schröder et al. FEBS Lett 290:1-3, 1991). To date, six mutations have been detected in patients with this form of GM2-gangliosidoses and include three missense, one nonsense and two small deletions. Mutations in the *GM2A* gene have been reported in patients from various ethnic groups including Saudi Arabian and Spanish from consanguineous families; and African-American and Laotian-Hmong with no apparent history of consanguinity.

Description of This Particular Test: The *GM2A* gene encodes a specific glycolipid binding protein, which is required for the lysosomal degradation of ganglioside GM2 by beta-hexosaminidase A. This test involves bidirectional DNA sequencing of all 4 exons and splice sites of the *GM2A* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. We will sequence any single or double exons in family members of patients with known mutation or to confirm previous results.

Reference Sequences: Genomic: **NC_000005.8** mRNA and Protein: **CCDS 4313.1**

Indications for Test: Patients with clinical features suggestive of GM2-Gangliosidosis and normal beta-hexosaminidase A and B isoenzymes are candidates for this test.

Sensitivity of Test: Unknown

Turn Around Time: Maximum of 40 calendar days, although many tests are completed in 20-30 days.

Specimen Requirements: See page 4 of the Requisition Form.

Price: Sequencing of all coding exons of the *GM2A* Gene: **\$440**

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x 4	83898 \$ 110	Sequencing x 4	83904 \$ 170
Separation x1	83894 \$ 30	Interpretation/Report x1	83912 \$ 60

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

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