Tay-Sachs Disease: *HEXA* Gene Deletion/Duplication

**Test Code:** NH  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

### Condition Description

Tay-Sachs disease is an autosomal recessive lysosomal storage disorder caused by accumulation of a fatty substance, called glycosphingolipid GM2 ganglioside, in the lysosomes. The fatty GM2 ganglioside substance is normally broken down in the lysosomes, by the enzyme hexosaminidase-A (*HEXA*). Loss of HEX A enzyme activity results in build up of the GM2 ganglioside in lysosomes, particularly in tissues of the central nervous system.

Tay Sachs disease is characterized by progressive neurodegeneration with symptoms including:

- seizures
- spasticity
- blindness
- loss of motor skills
- progressive muscle weakness
- decreased attentiveness
- increased startle reflex

A significant physical finding in persons with Tay-Sachs disease is a cherry red spot on the macula of the retina. Treatment of Tay-Sachs disease is supportive only and death usually occurs by 4 years of age. Variant forms of Tay-Sachs disease include chronic, juvenile, and adult-onset. These forms of *HEXA* deficiency are characterized by later onset and slower progression of variable neurodegenerative symptoms.

There are three protein components to the hexosaminidase complexes: the alpha subunit, the beta subunit and the GM2 ganglioside activator protein. Deficiency of the alpha subunit, due to mutations in the *HEXA* gene, results in deficiency of the hexosaminidase A complex and causes Tay-Sachs disease. Deficiency of the beta subunit, due to mutations in the *HEX B* gene, results in deficiency of both the beta-hexosaminidase A and B complexes and causes Sandhoff disease. Deficiency of the GM2 ganglioside activator protein, due to mutation in the *GM2A* gene, is associated with the rare AB variant form of GM2 gangliosidosis. Enzymatic analysis can distinguish between the GM2 gangliosidoses. Clinically, these diseases are indistinguishable.

Mutations in the *HEXA* gene cause Tay-Sachs disease. Targeted mutation detection can be performed to test for mutations common in the Ashkenazi Jewish population. For mutations not identified by this panel, sequencing of the *HEXA* gene must be performed. Diagnostic sequencing analysis of the *HEXA* gene coding region is available for Tay-Sachs disease patients and their at-risk relatives on a clinical basis.

For questions about testing for Tay-Sachs disease, call the Emory Genetics Laboratory at (404)778-8500 or (800)366-1502. For more information about lysosomal storage diseases, including management and treatment, call the Emory Lysosomal Storage Disease Center at (404)778-8565 or (800)200-1524.

### References:


### Genes

*HEXA*

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Tay Sachs Disease.
- Follow up of individuals with a positive/borderline biochemical carrier screening test.
- Prenatal testing for known familial mutations.
- Assessment of carrier status in high risk family members with known mutations.

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### Detection

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Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations.

Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Please submit copies of diagnostic biochemical test results along with the sample. Contact the laboratory if further information is needed. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Ashkenazi Jewish Carrier Screen (AJ) is available using targeted mutation analysis.
- Mutation Analysis for Pseudodeficiency Allele (GU) may be available upon request.
- Tay-Sachs Disease HEX A Enzyme Assay (HA) is available to establish a biochemical diagnosis.
- Sandhoff Disease: HEXB Gene Sequencing (DA).
- Lysosomal Enzyme Screening Panel (LS).
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.