

Gaucher Disease *via* GBA Gene Sequencing -- Test #479

Brief Description of Clinical Features: Gaucher Disease (GD, OMIM 230800) is one of several disorders of sphingolipid degradation, known as sphingolipidoses. Each sphingolipidosis is associated with defects of a specific lysosomal enzyme or other protein involved in sphingolipid degradation with subsequent accumulation of substrate in one or more organs. In patients with GD, a defective acid beta-glucocerebrosidase (GlcCer) enzyme results in the progressive accumulation of glucosylceramide (GlcCer) in reticuloendothelial cells with subsequent damage to various organs, including the liver, spleen, bone marrow, lungs and central nervous system (Brady et al Biochem Biophys Res Commun 18:221–225, 1965). Three GD Types (I, II and III) can be distinguished, according to the presence or absence of central nervous system abnormalities, age of onset, severity and progression. The earliest manifestations of GD are usually hematological abnormalities due to hypersplenism. Additional features are variable and include cytopenia, splenomegaly and bone fractures. GD patients are also classified using the Zimran Severity Score Index (Zimran et al. Medicine, Baltimore, 71:337-353, 1992). GD occurs in diverse ethnic groups, with an estimate incidence of 1 in 20,000 worldwide. It is however, most prevalent in the Ashkenazi Jewish populations (Beutler et al. Am J Hum Genet 52:85-88, 1993). See also the National Gaucher Foundation at (<http://www.gaucherdisease.org>).

Genetics: Types I, II and III GD are inherited with an autosomal recessive manner; they are caused by mutations in the glucocerebrosidase (*GBA*) gene (Tsuji et al. N Engl J Med 316:570-575, 1987). Over 300 mutations, distributed along the entire coding region of the gene have been detected in patients with GD. Homozygous mutations in families with or without history of consanguinity and compound heterozygous mutations were detected. Most mutations were unique to single families and include missense, nonsense, splicing, small insertions/deletions and indels. Gross insertions/deletions and complex rearrangements appear to be rare.

Description of This Particular Test: The *GBA* gene encodes for the enzyme acid beta-glucocerebrosidase, which catalyses the hydrolysis of glucocerebroside to ceramide and glucose. This test involves bidirectional DNA sequencing of all 11 coding exons and splice sites of the *GBA* 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_000001.9** mRNA and protein: **CCDS 1102.1**

Indications for Test: Patients with GD and heterozygous carrier relatives are candidates.

Sensitivity of Test: This test detects *GBA* mutations in ~ 99% of patients with Gaucher Disease Types I (OMIM 230800), II (OMIM 230900) and III (OMIM 231000) (Pastores and Hughes, GeneReviews, 2008, www.genetests.org).

Turn Around Time: Maximum of 40 calendar days, although many tests are completed in 3-4 weeks.

Specimen Requirements: See page 4 of the Requisition Form.

Price: Sequencing of all coding exons of the GBA Gene: \$ 630

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x3	83898 \$ 110	Sequencing x10	83904 \$ 350
Separation x1	83894 \$ 30	Interpretation/Report x1	83912 \$ 70

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

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