

**Mucopolysaccharidosis Type IIIB / Sanfilippo Syndrome B
 via *NAGLU* Gene Sequencing --Test #484**

Brief Description of Disorder: Mucopolysaccharidoses Type III (MPS III, Sanfilippo syndrome) are a group of inherited disorders caused by a deficiency in any of four lysosomal enzymes involved in the stepwise degradation of the glycosaminoglycan heparan sulfate. Enzyme deficiency results in progressive storage of heparan sulfate primarily in the central nervous system, leading to severe neurodegeneration and developmental delay. Age of onset for MPS III is usually between 2- 6 years and death usually occurs by the second or third decade of life. Symptoms typically begin with an episode of hyperactivity and aggressive behavior and progress to severe behavioral and sleep disturbances, hearing and visual defects, and mental retardation. Somatic involvement is usually mild and consists of hepatomegaly, dwarfism, joint stiffness, and coarse facial features (Neufeld and Muenzer In Scriver eds, 8th ed:3421-3452, 2001). MPS III are characterized by great clinical heterogeneity, even between sibs, in regard to age of onset, severity and clinical course. MPSIII are subdivided, on the basis of the specific enzyme deficiency, into four subtypes (IIIA, B, C, and D). Deficiency of the alpha-N-acetylglucosaminidase enzyme causes MPS IIIB (OMIM 252920). See also the National MPS Society at (www.mpssociety.org).

Genetics: MPS IIIB is an autosomal recessive disease caused by mutations in the *NAGLU* gene (Zhao et al. Am J Hum Genet 57:A185, 1995). About 120 mutations have been reported in patients from various ethnic populations. They include missense, nonsense, splicing, and small insertions or deletions mutations. Gross deletions and complex rearrangements are rare. As in the case of other MPS III most mutations are private, and the same mutations may result in varying severity among members of the same family (Beesley et al. J Med Genet 35:910-914, 1998). The c.700C>T (p.R234C) mutation is most common in Portuguese and Spanish populations and appears to have originated in the Iberian Peninsula (Mangas et al. Clin Genet 73:251-256, 2008).

Description of This Particular Test: The *NAGLU* gene encodes Alpha-N-acetylglucosaminidase. This test involves bidirectional DNA sequencing of all 6 exons and splice sites of the *NAGLU* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. As indicated, we will also sequence one (Test #100) or two (Test #200) exons in family members of patients with known mutations or to confirm research results (\$190-340).

Reference Sequences: Genomic: **NC_000017.10** mRNA: **NM_000263.3** Protein: **NP_000254.2 (CCDS 11427.1)**

Indications for Test: Patients with symptoms suggestive of MPS III, increased heparan sulfate excretion in urine, and reduced Alpha-N-acetylglucosaminidase activity; and potential heterozygous carriers.

Sensitivity of Test: Unknown.

Turnaround 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 *NAGLU* Gene: \$ 740

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x 12	83898 \$ 200	Sequencing x 12	83904 \$ 320
Separation x1	83894 \$ 60	Interpretation/Report x1	83912 \$ 90

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

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