

**Mucopolysaccharidosis Type IIIA / Sanfilippo Syndrome A  
 via *SGSH* Gene Sequencing -- Test #459**

**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 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). MPS IIIA (OMIM 252900) is usually the most severe. See also the National MPS Society at ([www.mpssociety.org](http://www.mpssociety.org)).

**Genetics:** MPS IIIA is inherited in an autosomal recessive manner and is caused by mutations in the *SGSH* gene (Scott et al. Nat Genet 11:465-467, 1995). To date, over 80 mutations have been reported in patients from various ethnic populations. Although most mutations are missense, a few nonsense, splicing, small insertions or deletions mutations have been reported. Gross deletions or complex rearrangements have not been reported. Clear genotype-phenotype correlations have not been established because most mutations are private (Yogalingam and Hopwood Hum Mutat 18:264-281, 2001), and because strong correlations between specific mutations and enzyme activity have not been observed (Beesley et al. J Med Genet 37:704-707, 2000).

**Description of This Particular Test:** The *SGSH* gene encodes the heparan N-sulfatase. This test involves bidirectional DNA sequencing of all 8 exons and splice sites of the *SGSH* 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\_000199.3 Protein: NP\_000190.1 (CCDS11770.1)

**Indications for Test:** Patients with symptoms suggestive of MPS III, increased heparan sulfate excretion in urine, and reduced heparan N-sulfatase 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 *SGSH* Gene: \$ 710

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x 11	83898 \$ 190	Sequencing x 11	83904 \$ 290
Separation x1	83894 \$ 60	Interpretation/Report x1	83912 \$ 100

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

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