

**Mucopolysaccharidosis Type IIIC / Sanfilippo Syndrome C
 via HGSNAT Gene Sequencing --Test #458**

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). Deficiency of the acetyl-CoA:alpha-glucosaminide N-acetyltransferase causes MPS IIIC (OMIM 252930). See also the National MPS Society at (www.mpsociety.org).

Genetics: MPS IIIC is inherited in an autosomal recessive manner and is caused by mutations in the *HGSNAT* gene (Hrebicek et al. Am J Hum Genet 79:807–819, 2006; Fan et al. Am J Hum Genet 79:738–744, 2006). Over 50 mutations have been reported in patients from various ethnic populations, and include missense, nonsense, splicing, and small insertions or deletions. Gross deletions and complex rearrangements were rare. Patients with two nonsense mutations usually develop a severe phenotype (Ruijter et al. Mol Genet Metab 93:104-111, 2008).

Description of This Particular Test: The *HGSNAT* gene encodes the acetyl-CoA:alpha-glucosaminide N-acetyltransferase. This test involves bidirectional DNA sequencing of all 18 exons and splice sites of the *HGSNAT* 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_000008.9 mRNA: NM_152419.2 Protein: NP_689632.2 CCDS: 47852.1

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

Sensitivity of Test: This Test is expected to detect ~ 90% of *HGSNAT* mutations (Hrebicek, 2006).

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 <i>HGSNAT</i> Gene:	\$ 960
CPT Codes:		
Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1 83891 \$ 40
Amplification x17	83898 \$ 280	Sequencing x17 83904 \$ 420
Separation x1	83894 \$ 80	Interpretation/Report x1 83912 \$ 110

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

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