

**Mucopolysaccharidosis Type IIID / Sanfilippo Syndrome D  
 via GNS Gene Sequencing --Test #456**

**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 N-acetylglucosamine-6-sulfatase enzyme causes MPS IIID (OMIM 252940), which is the least common of the four subtypes. See also the National MPS Society at ([www.mppsociety.org](http://www.mppsociety.org)).

**Genetics:** MPS IIID is inherited with an autosomal recessive manner and is caused by mutations in the *GNS* gene (Beesley et al. J Med Genet 40:192-194, 2003; Mok et al. Genomics 81:1-5, 2003). To date, ~10 mutations have been reported in patients from various ethnic populations. Most mutations are predicted to result in protein truncation and include nonsense, splicing, small insertions, small deletions and one gross deletion. In particular, no missense mutations have yet been reported for MPSIIID. Clear genotype-phenotype correlations have not been established because the same mutation may result in varying severity even among siblings (Jansen et al. Arch Neurol 64:1629-1634, 2007).

**Description of This Particular Test:** The *GNS* gene encodes the N-acetylglucosamine-6-sulfatase enzyme. This test involves bidirectional DNA sequencing of all 14 exons and splice sites of the *GNS* 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\_000012.10** mRNA: **NM\_002076.2** Protein: **NP\_002067.1** CCDS: **8970.1**

**Indications for Test:** Patients with symptoms suggestive of MPS III, increased heparan sulfate excretion in urine, and reduced N-acetylglucosamine-6-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 GNS Gene: \$ 880**

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x 15	83898 \$ 260	Sequencing x 15	83904 \$ 380
Separation x1	83894 \$ 70	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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