

## Mucopolysaccharidosis Type IIID: GNS Gene Deletion/Duplication

**Test Code:** IK

**Turnaround time:** 2 weeks

**CPT Codes:** 81228 x1

### Condition Description

Mucopolysaccharidosis type IIID (MPS IIID, Sanfilippo syndrome type D) is a member of a group of inherited metabolic disorders collectively termed mucopolysaccharidoses (MPSs). The MPSs are caused by a deficiency of lysosomal enzymes required for the degradation of mucopolysaccharides or glycosaminoglycans (GAGs) within the lysosome. When functioning normally, the lysosomal enzymes break down these GAGs, however when the enzyme is deficient, the GAGs build up in the lysosomes causing damage to the body's tissues. The MPSs share a chronic progressive course with multisystem involvement, characteristic physical features, laboratory findings, and radiographic abnormalities.

MPS IIID is an autosomal recessive disorder caused by a deficiency of the N-acetylglucosamine 6-sulfatase (GNS) enzyme and build up of heparin sulfate. Clinical features of MPS IIID include hyperactivity, aggressiveness, and developmental delays. Mental abilities decline as the disease progresses. Involvement of other organ systems tends to be mild and dysmorphic features are subtle than those observed in other types of mucopolysaccharidosis [1]. MPS IIID is caused by mutations in the *GNS* gene, but the disorder is clinically indistinguishable from MPS IIIA, MPS IIIB, and MPS IIIC, which are caused by mutations in other genes. All four forms of MPS III result in buildup of the same GAG, heparin sulfate. Diagnostic sequencing analysis of the *GNS* gene coding region is available for MPS type IIID patients and their at-risk relatives on a clinical basis.

For questions about testing for MPS IIID, call EGL Genetics at 470-378-2200. For further clinical information about lysosomal storage diseases, including management and treatment, call the Emory Lysosomal Storage Disease Center at (404) 778-8565 or (800) 200-1524.

Visit [www.ThinkGenetic.com](http://www.ThinkGenetic.com) for patient-friendly information on [mucopolysaccharidosis type III](#).

### References:

- 1). Muenzer, J., The mucopolysaccharidoses: a heterogeneous group of disorders with variable pediatric presentations. *J Pediatr*, 2004. 144(5 Suppl): p. S27-34.
- 2). Beesley, C.E., D. Burke, M. Jackson, A. Vellodi, B.G. Winchester, and E.P. Young, Sanfilippo syndrome type D: identification of the first mutation in the N-acetylglucosamine-6-sulphatase gene. *J Med Genet*, 2003. 40(3): p. 192-4.
- 3). Beesley, C.E., D. Concolino, M. Filocamo, B.G. Winchester, and P. Strisciuglio, Identification and characterisation of an 8.7kb deletion and a novel nonsense mutation in two Italian families with Sanfilippo syndrome type D (mucopolysaccharidosis IIID). *Mol Genet Metab*, 2006.
- 4). Mok, A., H. Cao, and R.A. Hegele, Genomic basis of mucopolysaccharidosis type IIID (MIM 252940) revealed by sequencing of GNS encoding N-acetylglucosamine-6-sulfatase. *Genomics*, 2003. 81(1): p. 1-5

### Genes

[GNS](#)

### Indications

- Confirmation of a clinical diagnosis of MPS IIID
- Prenatal testing for known familial mutations.
- Assessment of carrier status in high risk family members known mutation analysis.

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

### Detection

Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

### Specimen Requirements

**Submit only 1 of the following specimen types**

#### Type: Whole Blood (EDTA)

##### Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children ( 2 years of age to 10 years old): 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

##### Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

#### Type: DNA, Isolated

**Specimen Requirements:**

Microtainer

3µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside EGL Genetics, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.

**Related Tests**

- Mucopolysaccharide screen (urine GAG) (GA)
- Gene Sequencing for MPS IIIA (AW) and MPS IIIB (BB)
- Known mutation analysis (Custom Diagnostics) is available to test family members.
- Prenatal testing is available for known familial mutations only. Please call the Laboratory Genetic Counselor for specific requirements for prenatal testing before collecting a fetal sample.