Mucopolysaccharidosis Type III: \textit{SGSH}, \textit{GNS}, \textit{HGSNAT}, and \textit{NAGLU} Gene Deletion/Duplication Panel

<table>
<thead>
<tr>
<th>Test Code:</th>
<th>HV</th>
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<tbody>
<tr>
<td>Turnaround time:</td>
<td>2 weeks</td>
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<tr>
<td>CPT Codes:</td>
<td>81228 x1</td>
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## Condition Description

Mucopolysaccharidosis type III (MPS III, Sanfilippo syndrome), is a member of a group of inherited metabolic disorders collectively termed mucopolysaccharidoses (MPS's). The MPS's are caused by a deficiency of lysosomal enzymes required for the degradation of mucopolysaccharides or glycosaminoglycans (GAGs) within the lysosome [1]. 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 MPS's share a chronic progressive course with multisystem involvement and characteristic physical features such as coarse facies, hypertelorism, and coarse hair. The MPS patients are also characterized by developmental regression, hepatosplenomegaly and characteristic laboratory and radiographic abnormalities.

Clinical features of MPS III are similar to other MPS's and include hyperactivity, aggressiveness, and developmental delays in childhood. Mental abilities decline as the disease progresses. Involvement of other organ systems tends to be mild and dysmorphic features are more subtle than those observed in other type of mucopolysaccharidosis [1].

MPS III is caused by a deficiency of any of four lysosomal membrane enzymes, which leads to impaired degradation of heparan sulfate. The forms of MPS III are clinically indistinguishable each other and are caused by mutations in distinct genes. All four forms of MPS III result in buildup of the same GAG, heparin sulfate.

- MPS IIIA is caused by deficiency of the enzyme heparan N-sulfatase, encoded by the gene \textit{SGSH}.
- MPS IIIB is caused by deficiency of the enzyme alpha-N-acetylglucosaminidase, encoded by the gene \textit{NAGLU}.
- MPS IIIC is caused by deficiency of the enzyme heparin-alpha-glucosaminide N-acetyltransferase (N-acetyltransferase), encoded by the gene \textit{HGSNAT}.
- MPS IIID is caused by deficiency of the enzyme N-acetylglucosamine 6-sulfatase (N-acetyltransferase), encoded by the gene \textit{GNS}.

Diagnostic sequencing analysis of the panel of genes associated with MPS III is available for patients with a clinical diagnosis who have not had a fibroblast enzyme study to identify the specific subtype (FQ).

For questions about testing for MPS III, call the Emory Genetics Laboratory 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 \texttt{www.ThinkGenetic.com} for patient-friendly information on mucopolysaccharidosis type III.

References:

## Genes

\texttt{GNS, HGSNAT, NAGLU, SGSH}

## Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of MPS III when enzyme activity studies have not been obtained to identify the specific subtype.
- Carrier testing in adults with a family history of MPS III

## 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.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

## Detection

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

Prevalence: The estimated prevalence of all lysosomal storage disorders is 2-5 per 100,000. The prevalence of MPS III is not specifically known, but is likely to be rare and may vary by ethnicity.
Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow top) tube:
- Infants (<2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection 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 of Emory Genetics Laboratory, 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)
- Known mutation analysis (Custom Diagnostics) is available to test family members if mutations are identified by sequencing
- 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.