Mucopolysaccharidosis Type IIIA: \textit{SGSH} Gene Deletion/Duplication

\textbf{Test Code: HX}
\textbf{Turnaround time:} 2 weeks
\textbf{CPT Codes:} 81228 x1

\section*{Condition Description}

Mucopolysaccharidosis type IIIA (MPS IIIA, Sanfilippo syndrome type A), 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 IIIA is an autosomal recessive condition caused by a deficiency of the enzyme heparan N-sulfatase.

Clinical features of MPS IIIA 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 subtle than those observed in other type of mucopolysaccharidosis [1].

MPS IIIA is caused by mutations in the \textit{SGSH} gene, but is clinically indistinguishable from MPS IIIB, MPS IIC, and MPS IIID, 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 \textit{SGSH} gene coding region is available for MPS type IIIA patients and their at-risk relatives on a clinical basis.

For questions about testing for MPS IIID, 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 [www.ThinkGenetic.com](http://www.ThinkGenetic.com) for patient-friendly information on mucopolysaccharidosis type III.

\section*{References:}

\section*{Genes}
\textbf{SGSH}

\section*{Indications}

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

\section*{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.

\section*{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.

\section*{Specimen Requirements}

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

\section*{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 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 IIIB (BB) and MPS IIID (BH)
- 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.