Mucopolysaccharidosis Type IIIC: HGSNAT Gene Deletion/Duplication

Condition Description

Mucopolysaccharidosis type IIIC (MPS IIIC, Sanfilippo syndrome type C), 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 [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 MPSs 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 IIIC are similar to other MPSs 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 IIIC is caused by a deficiency of the lysosomal membrane enzyme heparin-alpha-glucosaminide N-acetyltransferase (N-acetyltransferase), which leads to impaired degradation of heparan sulfate. MPS IIIC is caused by mutations in the HGSNAT gene [2] (also known as the TMEM76 gene), but is clinically indistinguishable from MPS IIIA, MPS IIIB, 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 HGSNAT gene coding region is available for MPS type IIIC patients and their at-risk relatives (FN).

For questions about testing for MPS IIIC, 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 for patient-friendly information on mucopolysaccharidosis type III.

References:

Genes
HGSNAT

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of MPS IIIC.
- Carrier testing in adults with a family history of MPS IIIC

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 be interpreted in the context of the patients clinical and/or biochemical phenotype.

Specimen Requirements

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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Mucopolysaccharide screen (urine GAG) (GA)
- Gene sequencing for the MPS III gene sequencing panel when enzyme testing has not been performed
- Targeted 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 before collecting a fetal sample.