Mucolipidosis Type II: \textit{GNPTAB} Gene Deletion/Duplication

| Test Code: LJ | Turnaround time: 2 weeks | CPT Codes: 81228 x1 |

**Condition Description**

Mucolipidosis II (ML II or I-cell disease) is described as a Hurler-like lysosomal storage disorder with severe clinical and radiologic features. Leroy et al. (1970) first described this condition and named it I-cell disease, for inclusion cell disease, reflecting the buildup or inclusions noticeable in the lysosomes. The accumulation of material in the lysosomes results from the inability of the lysosomal enzymes to enter the lysosome for normal degradation. A biochemical marker signal is required for proper trafficking of the lysosomal enzymes, from the site of production in the endoplasmic reticulum to the lysosome itself. This marker was identified as a mannose-6-phosphate residue on the lysosomal enzyme that interacts with a specific receptor on the lysosomal membrane, which then triggers entry into the lysosome. The biochemical defect in I-cell disease is due to the lack of the enzyme (abbreviated GlcNAc-1-P) involved in the addition of the mannose-6-phosphate residue.

Clinical symptoms may be noticeable from infancy and may include: congenital dislocation of the hip, thoracic deformities, hernia, and hyperplastic gums which are evident soon after birth. Other symptoms may include delayed psychomotor development, clear corneas, and restricted joint mobility.

Mutations in the \textit{GNPTAB} gene cause a deficiency of the enzyme GlcNAc-1-P. Diagnostic sequencing analysis of the \textit{GNPTAB} gene coding region is available for mucolipidosis II patients and their at-risk relatives on a clinical basis.

For questions about testing for ML II, call EGL Genetics at (470) 378-2200 or (855) 381-7447. 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.

**References:**

**Genes**

\textbf{GNPTAB}

**Indications**

- Confirmation of clinical diagnosis of ML II disease
- Prenatal testing for known familial mutation(s).
- 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. 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 patient's 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) 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**

- Known Mutation Analysis (KM) 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.