Alpha-N-acetylgalactosaminidase (Alpha-NAGA) Deficiency: NAGA Gene Sequencing

**Condition Description**

Mutations in the NAGA gene (22q13.2) cause a deficiency of the lysosomal enzyme, alpha-N-acetylgalactosaminidase (?-NAGA). A spectrum of diseases is caused by deficiency of ?-NAGA; Schindler disease, at the more severe end, and Kanzaki disease at the milder end. Patients with ?-NAGA deficiency were found to have two mutations each in the NAGA gene, consistent with an autosomal recessive inheritance pattern. Schindler disease has infantile onset and is characterized by neuroaxonal dystrophy without visceral involvement or dysmorphism, seizures, and intellectual disability. Kanzaki disease is an adult onset condition characterized by slight facial coarseness, mild intellectual disability, disseminated angiokeratoma, but no neurological symptoms. Additional cases have been described in this spectrum with various degrees of psychomotor delays, behavioral problems, and epilepsy.

References:

- OMIM #104170: NAGA gene
- OMIM #609241: Schindler disease
- OMIM #609242: Kanzaki disease

**Indications**

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of ?-NAGA deficiency
- Carrier testing in adults with a family history of ?-NAGA deficiency

**Methodology**

PCR amplification of 9 exons contained in the NAGA gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

**Detection**

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%

**Specimen Requirements**

*Submit only 1 of the following specimen types*

**Type: Saliva**

**Specimen Requirements:**
Oragene™ Saliva Collection Kit
Orangene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**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 uncapped 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
8µg
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, if appropriate. Contact the laboratory if further information is needed.

**Related Tests**
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available to adult couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.