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 dysmorphosis, 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

### Genes

NAGA

### 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

* 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, 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.