

NGLY1 Deficiency: NGLY1 Gene Sequencing

Test Code: SGLY1

Turnaround time: 6 weeks

CPT Codes: 81479 x1

Condition Description

NGLY1 deficiency is a novel autosomal recessive disorder of the endoplasmic reticulum–associated degradation pathway associated with neurological dysfunction, abnormal tear production, and liver disease. The enzyme N-glycanase 1 (*NGLY1*), also known as peptide: N-glycanase (PNGase, EC 3.5.1.52), catalyzes protein deglycosylation by cleaving the β -aspartyl glycosylamine bond of N-linked glycoproteins with the subsequent release of intact N-glycan species. Evidence suggests that *NGLY1* participates as a key cytoplasmic component of the endoplasmic reticulum–associated degradation (ERAD) machinery along with the AAA ATPase complex p97. The ERAD pathway is a mechanism for identifying and degrading misfolded glycoproteins. N-glycans that are high in mannose content act as quality control tags for proteins in the early stages of the secretory pathway. Misfolded glycoproteins are detected by ER luminal lectins and are then translocated to the cytosol via the ERAD machinery to be subsequently degraded by cytosolic enzymes, including *NGLY1*. The majority of patients detected to date carry a specific nonsense mutation that appears to be associated with severe disease. The phenotypic spectrum is likely to enlarge as cases with a broader range of mutations are detected. *NGLY1* deficiency is caused by mutations in the *NGLY1* gene.

Reference:

- Enns GM, et al. (2014) *Genet Med*.

Genes

[NGLY1](#)

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of *NGLY1* deficiency.

Methodology

For Sanger sequencing:

PCR amplification of 10 exons contained in the *NGLY1* 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

Full Gene Sequencing

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 clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Saliva

Specimen Requirements:

Oragene™ Saliva Collection Kit

Oragene™ 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: 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.

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 unclotted 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.

Related Tests

- Congenital Disorders of Glycosylation Gene Sequencing and Deletion/Duplication Panel