

Mucopolysaccharidosis Type IVA: GALNS Gene Sequencing

Test Code: BU

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

Mucopolysaccharidosis type IV A (Morquio syndrome, MPS IV A) is a member of a group of inherited metabolic disorders collectively termed mucopolysaccharidoses (MPSs). The MPS's are caused by a deficiency of lysosomal enzymes required for the degradation of mucopolysaccharides or glycosaminoglycans (GAGs). Morquio syndrome type IVA is caused by deficiency of galactosamine-6-sulfatase (N-acetyl-galactosamine-6-sulfate sulfatase deficiency). Deficiency of this enzyme leads to the accumulation of the GAG, keratan sulfate, in the lysosomes.

Symptoms of Morquio syndrome include the excretion of specific urinary glycosaminoglycans and skeletal abnormalities. Most individuals affected by Morquio syndrome do not have coarse facial features or mental retardation. Skeletal manifestations of Morquio syndrome include: odontoid hypoplasia, a striking short trunk dwarfism, and genu valgus. Compared to other patients with MPS, those with Morquio syndrome tend to have greater spine involvement with scoliosis, kyphosis, and severe gibbus, as well as platyspondyly, rib flaring, pectus carinatum, and ligamentous laxity. In earlier clinical descriptions, MPS Type IVA was considered to have more severe manifestations than type IVB. However, with the ability to differentiate between types A and B by enzyme analysis, it is understood that significant variability in clinical expression exists within both groups. No clear clinical differentiation between Morquio syndrome type IVA and IVB exists.

Mutations to the *GALNS* gene cause deficiency of galactosamine-6-sulfatase. Diagnostic sequencing analysis of the *GALNS* gene coding region is available for MPS IV A patients and their at-risk relatives on a clinical basis.

For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array (LX).

For questions about testing for MPS IV A, call EGL Genetics at (470) 378-2200 or (855) 831-7447. 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:

- 1). Tomatsu S, Fukuda S, Cooper A, Wraith JE, Rezvi GMM, Yamagishi A, Yamada N, Kato Z, Isogai K, Sukegawa K, Kondo N, Suzuki Y, Shimozawa N, Orii T. Mucopolysaccharidosis IVA: identification of a common missense mutation I113F in the N-acetylgalactosamine-6-sulfate sulfatase gene. *Am. J. Hum. Genet.* 57: 556-563, 1995.
- 2). Fukuda S, Tomatsu S, Masuno M, Ogawa T, Yamagishi A, Rezvi GMM, Sukegawa K, Shimozawa N, Suzuki Y, Kondo N, Imaizumi K, Kuroki Y, Okabe T, Orii T. Mucopolysaccharidosis IVA: submicroscopic deletion of 16q24.3 and a novel R386C mutation of N-acetylgalactosamine-6-sulfate sulfatase gene in a classical Morquio disease. *Hum. Mutat.* 7: 123-134, 1996.
- 3). Tomatsu, S.; Montano, A. M.; Nishioka, T.; Gutierrez, M. A.; Pena, O. M.; Trandafirescu, G. G.; Lopez, P.; Yamaguchi, S.; Noguchi, A.; Orii, T. Mutation and polymorphism spectrum of the *GALNS* gene in mucopolysaccharidosis IVA (Morquio A). *Hum. Mutat.* 26: 500-512, 2005.

Genes

[GALNS](#)

Indications

- Confirmation of a clinical diagnosis of MPS IV A Disease
- Prenatal testing for known familial mutation(s).
- Assessment of carrier status in high risk family members known mutation analysis.

Methodology

PCR amplification of 14 exons contained in the *GALNS* gene coding region will be performed on patient genomic DNA. Direct sequencing of amplification products is performed in both the forward and reverse directions using automated fluorescence dideoxy sequencing methods. Patient gene sequences are compared to a normal reference sequence. Sequence variations are then 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. Large deletions are not detected by this analysis. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Detection

Full Gene Sequencing:

Clinical Sensitivity: Tomatsu S, et al. reported a summary of 148 mutations found in affected patients (84% of alleles interrogated) [3]

Analytical Sensitivity: ~99%

Prevalence: The estimated prevalence of all lysosomal storage disorders is 2-5 per 100,000. The prevalence of MPS IV is not specifically known, but is likely to be rare and may vary by ethnicity. 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

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: 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.

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. 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

- Mucopolysaccharide screen (urine GAG) (GA)
- Known mutation analysis (Custom Diagnostics) is available to test family members.
- Deletion/duplication analysis for the *GALNS* gene is available separately for individuals where mutations are not identified by sequence analysis.
- 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.