

## Mucopolysaccharidosis Type IVA / Morquio Type A Disease via GALNS Gene Sequencing --Test #455

**Brief Description of Disorder:** The mucopolysaccharidoses (MPS) are a group of inherited disorders caused by defects in lysosomal enzymes responsible for the degradation of glycosaminoglycans (GAGs). Each enzyme deficiency results in progressive storage of distinct GAGs in multiple organ systems and subsequent abnormalities. Although MPS share several symptoms, including physical and mental developmental abnormalities, they may differ even within the same enzyme deficiency. MPS are classified in seven groups on the basis of clinical symptoms (Types I, II, III, IV, VI, VII, and IX). Defects in eleven different enzymes have been associated with the various MPS. **MPS IVA** (Morquio Type A disease, OMIM 253000), is caused by deficiency in the N-acetylgalactosamine-6-sulfatase enzyme and subsequent accumulation of keratin and chondroitin 6-sulfates, mainly in the cornea and cartilage, leading to distinguishing skeletal abnormalities. MPS IVA is distinguished from other MPS by a spondyloepiphyseal dysplasia and normal intelligence. In the classical and most severe form, symptoms begin between 1-4 years of age and include tendency to fall, coarse features, dwarfism with short trunk, osteoporosis, corneal deposits, hearing impairment, and hepatomegaly. A milder form of MPS IVA is characterized by mild bone and somatic involvement with survival to 60 years of age and normal quality of life (Neufeld and Muenzer In Scriver eds, 8th ed:3421-3452, 2001).

**Genetics:** MPS IVA is an autosomal recessive disease that results from mutations in the *GALNS* gene (Fukuda et al. J Clin Invest 90:1049-1053, 1992). Over 150 mutations have been reported in patients from various ethnic populations. All types of mutations have been reported. However, the vast majority were missense and nonsense mutations. Of note, a substantial number of missense mutations occurred in large, not well conserved amino acids (Tomatsu et al. Hum Mutat 24:187-188, 2004). Several mutations were detected in specific populations. For example, a large rearrangement and two substitutions appear to be common only in patients of Japanese and British/Irish origin, respectively.

**Description of This Particular Test:** The *GALNS* gene encodes the N-acetylgalactosamine-6-sulfatase enzyme, which catalyzes the hydrolysis of keratin and chondroitin 6-sulfates. This test involves bidirectional DNA sequencing of all 14 exons and splice sites of the *GALNS* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. As indicated, we will also sequence one (Test #100) or two (Test #200) exons in family members of patients with known mutations or to confirm research results (\$190-340).

**Reference Sequences:** Genomic: NC\_000016.8 mRNA: NM\_000512.4 Protein: NP\_000503.1 (CCDS 10970.1)

**Indications for Test:** Patients with symptoms suggestive of MPS, increased keratin sulfate and chondroitin-6-sulfate excretion in urine, and reduced N-acetylgalactosamine-6-sulfatase enzyme activity; and potential heterozygous carriers.

**Sensitivity of Test:** Unknown.

**Turnaround Time:** Maximum of 40 calendar days, although many tests are completed in 20-30 days.

**Specimen Requirements:** See page 4 of the Requisition Form.

<b>Price:</b>	<b>Sequencing of all coding exons of the GALNS Gene:</b>	<b>\$840</b>
<b>CPT Codes:</b>		
Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1 83891 \$ 40
Amplification x14	83898 \$ 250	Sequencing x14 83904 \$ 370
Separation x1	83894 \$ 60	Interpretation/Report x1 83912 \$ 90

**Accreditation Info:** CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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