

Mucopolysaccharidosis Type IX via *HYALI* Gene Sequencing --Test #485

Brief Description of Disorder: The mucopolysaccharidoses (MPS) are a group of inherited disorders caused by defects in lysosomal enzymes responsible for 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 the clinical symptoms (Types I, II, III, IV, VI, VII, and IX). Defects in eleven different enzymes have been associated with the various MPS (Neufeld and Muenzer In Scriver eds, 8th ed:3421-3452, 2001). **MPS Type IX** (OMIM 601492) is caused by deficiency in the hyaluronidase enzyme and subsequent accumulation of lysosomal hyaluronan. The unique patient reported to date presented with short stature and periarticular soft-tissue masses accompanied by episodes of painful swelling that resolved within a 3-day period. These episodes started toward the end of the first decade of life. Visceral and mental development were normal (Natowicz et al. N Engl J Med 335:1029-1033, 1996).

Genetics: MPS IX is inherited in an autosomal recessive manner and is caused by mutations in the *HYALI* gene. To date, two mutations were identified in the patient reported by Natowicz et al. (Natowicz, 1996). The first is a missense mutation defined as c.1412G>A (p.Glu268Lys). The second mutation consists of a complex rearrangement defined as c.1361del37ins14 and predicted to result in premature protein termination (Triggs-Raine et al. PNAS 96:6296-6300, 1999).

Description of This Particular Test: The *HYALI* gene encodes the hyaluronidase enzyme, which catalyzes the degradation of hyaluronan, one of the main glycosaminoglycans of the extracellular matrix. This test involves bidirectional DNA sequencing of all 3 exons and splice sites of the *HYALI* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. As indicated, we will sequence one (Test #100) or two (Test #200) exons in family members of patients with known mutations or to confirm previous results.

Reference Sequences: Genomic: NC_000003.10 mRNA: NM_153281.1 Protein: NP_695013.1 (CCDS 2816.1)

Indications for Test: Patients with symptoms suggestive of MPS, increased plasma hyaluronan concentration, and reduced or complete deficiency of hyaluronidase enzyme activity; and potential heterozygous carriers.

Sensitivity of Test: Unknown, but *HYALI* mutations appear to be a rare cause of MPS.

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.

Price: Sequencing of all coding exons of the *HYALI* Gene: \$ 540

CPT Codes:

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|-------------------------|--------------|--------------------------|--------------|
| Sample Ascertainment x1 | 83890 \$ 30 | DNA Isolation x1 | 83891 \$ 40 |
| Amplification x 7 | 83898 \$ 140 | Sequencing x7 | 83904 \$ 210 |
| Separation x1 | 83894 \$ 40 | Interpretation/Report x1 | 83912 \$ 80 |

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

Contact: Dr. Khemissa Bejaoui, khemissa@preventiongenetics.com, www.preventiongenetics.com