

3-M Syndrome via *CUL7* Gene Sequencing (Test #624)

Brief Description of Clinical Features: 3-M syndrome (OMIM 273750) is an intrauterine growth retardation disorder characterized by pre- and postnatal growth retardation, a large head circumference, and a characteristic facial appearance including a prominent forehead, pointed triangular shaped face, a short upturned nose with anteverted nares, prominent mouth and lips and full eyebrows (van der Wal et al. Clin Dysmorphol 10:241-252, 2001; Marik et al. J Paediatr Child Health 38:419-422, 2002; Huber et al. Nat Genet 37:1119-1124, 2005). Additional findings include a short broad neck, prominent trapezii, deformed sternum, short thorax, square shoulders, winged scapulae, hyperlordosis, short fifth fingers, slender long bones with diaphyseal constriction, tall vertebral bodies, delayed bone age and prominent heels (van der Wal et al. 2001; Huber et al. 2005; Huber et al. Eur J Hum Genet 17:395-400, 2009).

Genetics: 3-M syndrome is an autosomal recessive disorder caused by mutations in the *CUL7* gene (Huber et al. 2005). The *CUL7* gene encodes cullin-7 protein, which plays a scaffold role in assembling an E3 ubiquitin ligase complex. This complex contains both the heterodimer of Skp1 and Fbx29 (also known as Fbw8) and the ROC1 RING-finger protein (Huber et al. 2005). A mix of missense, nonsense, frameshift, splicing, deletions and duplications mutations have been reported in *CUL7* (Huber et al. 2005; Huber et al. 2009)

Description of This Particular Test: This test involves bidirectional sequencing using genomic DNA of the 25 coding exons (exons 2-26) of the *CUL7* gene. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on each side are sequenced. As indicated, we will also perform sequencing of any single exon (Test #100) or pair of exons (Test #200) for family members of patients with known mutations and to confirm previous research results (\$190-340 charge).

Reference Sequences: Genomic: NC_000006.11 mRNA: NM_014780.4 Protein: NP_055595.2 (CCDS 4881.1)

Indications for Test: Candidates for this test are patients with symptoms consistent with 3-M syndrome and family members of patients who have known *CUL7* mutations.

Sensitivity of Test: The prevalence of the *CUL7* mutations is currently unknown. However, *CUL7* mutations account for ~84% of the 3-M syndrome reported cases (Huber et al. 2009).

Turnaround Time: Maximum of 40 calendar days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See page 4 of the Requisition Form.

Prices: Sequencing of *CUL7* gene \$ 1340

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x28	83898 \$ 420	Sequencing x28	83904 \$ 630
Separation x1	83894 \$ 100	Interpretation/Report x1	83912 \$ 120

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

Contact for Info: Dr. Ying Wang, ying.wang@preventiongenetics.com, www.preventiongenetics.com