3-m syndrome locus (7, 8). also, mutations

3-M syndrome (MIM: 612921) is pre- and post-natal growthrestriction with relatively common group of disorders involving the skeletalsystem, normal intelligence and distinctive facial features (1, 2). The three principle geneticists' 3-MSBN whofirst described the condition is Miller, McKusick, and Malvaux(3). 3-M syndromeis characterized by prominent heels, normal loose joints and, in some cases, radiological abnormal features (4).

Affected males with 3-M syndrome havehypogonadism, hypospadias and hypogonadism (5, 6). It is caused by pathogenicmutations in encoding cullin 7 (CUL7 MIM: 609577) were subsequentlyidentified as the primary cause of 3-M syndrome that revealed a locus onchromosome 6p21. 1. Obscurin-like protein 1 (OBSL1 MIM: 610991) gene on longarm of the chromosome 2 is the second 3-M syndrome locus (7, 8). Also, mutationsin coiled-coil domain containing protein 8 (CCDC8) have been reported as geneticcause of 3M syndrome (9). CUL7 is a structural protein and OBSL1 encodea cytoskeletal adaptor protein.

Exactly function of CCDC8 gene undetermined. However, the physical interaction of CCDC8 with CUL7 and OBSL1have potential role in the growth-regulatory pathways (10). 3-M syndrome is an autosomalrecessive growth disorder. On the other hand, The function of OBSL1gene ingrowth is doubtful. . It is acytoskeletal adaptor protein, like titinand myomesin proteins, which localises to the perinuclear region to maintainthe structural integrity of the cells with linking cytoskeletal proteins (11, 12). However, recent studies established that individuals with 3-M syndrome andOBSL1 mutations showed significant modulation of Insulin-like growth factorbinding protein 2 (IGFBP2 MIM: 146731) and IGFBP5 (MIM: 146734)expression(13).

Moreover, OBSL1 gene has a broader rolein the CUL7 ligase signaling ubiquitination Pathway with controls Golgi anddendrite morphogenesis (14). Knockdown siRNA studies demonstratedthat OBSL1 mutations led to reduction in CUL7 expression. (15) Therefore, it is possible that CUL7–SCFcomplex assistance with OBSL1 protean (16). OBSL1 also acts to binding Mitogen-activatedprotein kinase 11 (MAPK11) and MAPK14 in the cancer pathways (17). Although, there is only elementary knowledgeof OBSL1 and it is clear that further characterization is required to elucidatethe function of OBSL1 and specifically its impact on the regulation of human growth(18, 19).

For OBSL1, approximately half of the patients have the same commonnonsense mutation (c. 1273dupA, p. T425Nfs*40) (20). 3-M syndrome can bediagnosed using well-established molecular basis and prevalence has beendemonstrated in many populations.

3-M syndrome prevalence and spectrum areunknown in Iran. In the present study, we identifyand report for the first time an unreported nonsense mutation on OBSL1 genein an Iranian family with 3-M syndrome.