A novel nonsense mutation in the sedlin gene (SEDL) causes severe spondyloepiphyseal dysplasia tarda in a five-generation Chinese pedigree

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ABSTRACT. Spondyloepiphyseal dysplasia tarda (SEDT) is an X-linked recessive osteochondrodysplasia characterized by disproportionately short stature and degenerative joint disease. The objective of this study was to describe a novel nonsense mutation in the sedlin gene (SEDL) causing severe SEDT in a large Chinese pedigree. The clinical features of all affected individuals and female carriers were presented. Four affected males of the family were diagnosed with SEDT according to their clinical and radiological features. Direct DNA sequencing of SEDL was performed. Reverse-transcription polymerase chain reaction (RT-PCR) experiments of
total RNA from blood lymphocytes were performed to confirm the
defect in SEDL. DNA sequencing revealed that all of the affected males
carried a nonsense mutation (c.61G>T) in SEDL that has not been
previously reported. The c.61G>T mutation resulted in a premature
translation termination codon (GAG>TAG) at amino acid position
21 (p.E21*), and was predicted to initiate the degradation of mutant
transcripts through the nonsense-mediated mRNA decay pathway.
Two female carriers showed typical sequencing chromatograms
of a heterozygote. Following genetic counseling, individual IV7
gave birth to a healthy baby. Therefore, identification of the novel
nonsense mutation (c.61G>T) in the SEDT family enables carrier
detection, genetic counseling, and prenatal diagnosis. The detailed
genotype/phenotype descriptions contribute to the SEDL mutation
spectrum. The continued identification of mutations in SEDT patients
will greatly aid further elucidation of the role of the sedlin protein in
normal bone growth.

**Key words:** Spondyloepiphyseal dysplasia tarda; SEDL gene;
Nonsense mutation