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Whole exome sequencing implicates *PTCH1* and *COL17A1* genes in ossification of the posterior longitudinal ligament of the cervical spine in Chinese patients

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ABSTRACT. Ossification of the posterior longitudinal ligament (OPLL) of the cervical spine is a complex multifactorial disease. Patients with OPLL commonly present with symptoms in their 40s or 50s. The genetic basis of OPLL remains poorly understood. Exome capture combined with massively parallel DNA sequencing has been proposed as an efficient strategy to search for disease-causing genes of both monogenic and multigenic disorders. To identify candidate pathogenic genes associated with OPLL, we performed whole exome sequencing (WES) on two unrelated southern Chinese OPLL patients.

The entire DNA coding region of the candidate genes was amplified by PCR and Sanger sequenced. The common single nucleotide polymorphisms were analyzed by association studies. WES revealed p.T265S/*PTCH1*, p.P1232L/*PTCH1*, and p.T902S/*COL17A1* mutants in the two female cases with mixed OPLL. These were confirmed by Sanger sequencing. p.P1232L/*PTCH1*, p.N1374D/*COL17A1* and p.T902S/*COL17A1* were subsequently identified in three males with continuous OPLL and one female with mixed OPLL. The association studies indicated that the SNPs rs805698 and rs4918079 in *COL17A1* were significantly associated with OPLL. This study suggests that WES may be a practical approach to revealing significant genetic involvement in OPLL. Variants of the *PTCH1* and *COL17A1* genes may contribute to the development of OPLL.

Key words: Ossification of the posterior longitudinal ligament; Whole exome sequencing; Susceptible gene; *PTCH1*; *COL17A1*

