Transmembrane protein 100 (TMEM100) comprises 134 amino acid residues and is highly conserved among vertebrates. Tmem100 has been recently reported as a key factor in angiogenesis, pain transmission, and tumor suppression. Although the importance of TMEM100 function is well supported, few studies have elucidated its expression mechanism. In the current study, we found that activating transcription factor 6α, a transcription factor activated by endoplasmic reticulum (ER) stress, enhanced *Tmem100* promoter activity. Two ER stress response element-like motifs were identified in the mouse *Tmem100* promoter region. However, additional experiments using another type of ER stress inducer demonstrated that calcium signaling was more important than ER stress in the regulation of *TMEM100* expression. Intracellular calcium signaling controls biological processes such as cell proliferation and embryonic development. This study suggested that TMEM100 performs various functions in response to alterations in calcium signaling in addition to those in response to ER stress.

The expression of *Transmembrane Protein 100* is increased by alterations in calcium signaling rather than endoplasmic reticulum stress.