# Effect of TIMP1 transfection on PTEN expression in human kidney proximal tubular cells

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**ABSTRACT.** To explore the role of metalloproteinase-1 (TIMP-1) tissue inhibitor in the mechanisms of kidney aging, we observed the effects of sense and antisense transfection of *TIMP-1* and of metalloproteinase (MMP) inhibitors on phosphatase and tensin homolog (PTEN), vascular endothelial growth factor (VEGF), and Flk-1 expression in *TIMP-1* transgenic human proximal tubular epithelial cells (HKCs). Transfected HKCs were co-incubated with 100 µM MMP-2 and MMP-9 inhibitor III for 24 h to affect enzyme inhibition. *TIMP-1*, *MMP-2*, *MMP-9*, *PTEN*, *VEGF*, and *Flk-1* mRNA expression was detected by reverse transcription-polymerase chain reaction. PTEN, VEGF, and Flk-1 protein expression in cells of each experimental group was measured by indirect immunofluorescence. We found that PTEN expression was up-regulated ($P < 0.05$) in the sense *TIMP-1*-transfected group ($P < 0.05$) compared with the non-transfected and empty vector groups, and that expression of VEGF and Flk-1 was down-regulated ($P < 0.05$). In contrast, the antisense *TIMP-1* transgenic group showed the opposite results ($P < 0.05$). No significant differences

 

in expression of PTEN, VEGF, or Flk-1 were observed among the MMP-2/MMP-9 inhibitor III, non-transfected, and empty vector groups ($P > 0.05$). These results suggest that in the progression of renal aging, high expression of TIMP-1 up-regulates PTEN expression through an MMP-independent pathway, and subsequently down-regulates the expression of VEGF and Flk-1, indicating that PTEN and TIMP-1 are involved in the aging-associated impairment of renal angiogenesis. Our study provides a theoretical basis for further exploration of the mechanism underlying TIMP-1 participation in renal aging progression.

**Key words:** TIMP-1; Kidney aging; Angiogenesis; PTEN

 