[P-8]

TIMP-2 Overexpression Suppresses Migraion, Invasiveness and Angiogenesis

Seong-Min Ahn, Yeowon Sohn[1], Yun-Soo Kim[2] and Aree Moon

College of Pharmacy, Duksung Women's University, Seoul 132-714, Korea
[1] KFDA
[2] KRIBB

An imbalance between matrix metalloproteinase (MMP)-2 and its endogenous inhibitor, tissue inhibitor of metalloproteinase (TIMP)-2 causes the degradation of the extracellular matrix associated with pathological events including invasion, metastasis and angiogenesis. Since TIMPs are secreted molecules, they have the potential to be used for gene therapy of certain tumors. In present study, we have studied the retrovirus-mediated delivery of TIMP-2 in H-ras MCF10A cells in which MMP-2 was shown to be responsible for the H-ras-induced invasive phenotype. PG13 cells, packaging cells, were infected with the recombinant retrovirus containing TIMP-2 gene (rRetTIMP-2). Recombinant retrovirus containing LacZ (rRetLacZ) was used as a control. Overexpression of TIMP-2 was detected in H-ras MCF10A cells infected by rRetTIMP-2 after 5 days in culture. Retroviral delivery of TIMP-2 in H-ras MCF10A cells caused a significant downregulation of MMP-2 in a dose-dependent manner as evidenced by Western blot and gelatin zymography. Migration and invasive phenotype H-ras MCF10A cells were markedly inhibited by rRetTIMP-2 infection compared to the cells infected with rRetLacZ. In addition, retroviral delivery of TIMP-2 efficiently inhibited angiogenesis of HUVECs dose-dependently as evidenced by in vitro tube formation assay. Taken together, we show that the downregulation of MMP-2 by TIMP-2 overexpression inhibits migrative and invasive properties of H-ras MCF10A cells and angiogenesis of HUVECs, suggesting a possible application for gene therapy to prevent and treat cancer.

Keyword : TIMP-2, retrovirus, gene therapy