Overexpression of FoxM1 is Associated with Tumor Progression in Patients with Renal Cell Carcinoma

Introduction and Objective: The Forkhead Box M1 (FoxM1) transcription factor has been shown to play important roles in regulating the expression of genes involved in cell proliferation, differentiation, and transformation. The present study was undertaken to investigate the expression of FoxM1 and its prognostic significance in renal cell carcinomas (RCC). Experiments in cell lines were also carried out.
Materials and Methods: Tumor tissue microarray was applied to examine expression of FoxM1 protein in archival kidney cancer samples from 150 patients and investigated its clinicopathologic significance. FoxM1 expression was knocked down by small interfering RNA in 786-0 and Caki-2 cells; proliferation migration, invasion, and angiogenesis were assayed.
Results: FoxM1 protein expression levels were positively correlated with primary tumor stage, distant metastasis, and histologic grade. Multivariate Cox analysis revealed that elevated FoxM1 expression was an independent prognostic factor for overall survival (P = 0.0012). Experimentally, we found that down-regulation of FoxM1 inhibited cell proliferation, decreased cell migration, and decreased invasion of cancer cells. Compared with control, FoxM1 small interfering RNA-transfected cells showed decreased expression of cyclin B, cyclin D1, and Cdk2. We also found that down-regulation of FoxM1 reduced the expression of matrix metalloproteinase-2 (MMP-2), MMP-9 and vascular endothelial growth factor, resulting in the inhibition of migration, invasion, and angiogenesis.
Conclusion: These results suggest that FoxM1 expression is likely to play important roles in RCC development and progression, and that FoxM1 is a prognostic biomarker and a promising therapeutic target for RCC.