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The siRNA cocktail targeting VEGF and HER2 inhibition on the proliferation and induced apoptosis of gastric cancer cell

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Abstract The aim of this study was to investigate the inhibitory effect of a siRNA cocktail targeting Vascular endothelial growth factor (VEGF) and Human epidermal growth factor receptor 2 (HER2) on cell proliferation, induced apoptosis and the expression of VEGF and HER2 in human gastric carcinoma cell. The silencing rate of predesigned siRNAs that targeted VEGF and HER2 was detected by Real-time Quantitative PCR (RT-QPCR) analysis. Furthermore, the best silencing siRNA that targeted VEGF and HER2 was prepared as a cocktail to co-knockdown VEGF and HER2 expression at both mRNA and protein levels which were detected by RT-QPCR and Western blot analysis. Cell proliferation inhibition rates were determined by CCK8 assay. The effect of siRNA cocktail on cell apoptosis was determined by flow cytometry. The migration inhibition of siRNA cocktail was analyzed by wound-healing assay. The ability of VEGF to induce endothelial cells to proliferate was examined in HUVECs by the method of tube formation assay. The predesigned siRNAs could inhibit VEGF and HER2 mRNA level. siRNA cocktail, and co-downregulation of VEGF and HER2 result in significant inhibition of gastric cancer growth and migration in vitro. The inhibition of VEGF and HER2 expressions can induce apoptosis of SGC-7901 cells.

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Introduction

Gastric cancer is one of the most common types of cancer and the second most common cause of cancer-related mortality worldwide [1, 2]. At present, conventional therapies for gastric cancer include resection, chemotherapy, and radiotherapy, but these measures are non-curative for those patients who are diagnosed with advanced gastric cancer. As a result, new therapeutic methods are needed urgently for more effective treatment of this aggressive malignancy. Biological therapy based on the molecular-targeted therapy is an emerging technology for gastric cancer to improve the quality of life and survival of patients.

RNA interference (RNAi) is a post-transcriptional process triggered by double-stranded RNA which leads to gene silencing in a sequence-specific manner through degradation of the corresponding mRNA.

Human epidermal growth factor receptor 2 (HER2), also known as ErbB-2, is a protein that in humans is encoded by the ERBB2 gene. HER2 is a member of the epidermal growth factor receptor (EGFR/ErbB) family. Its activation leads to a cascade of events promoting rapid cell growth, differentiation, survival, and migration [3]. Overexpression of HER2 has been found to induce tumorigenesis and to be involved in the pathogenesis of gastric cancer [4]. Amplification and overexpression of HER2 play an important role in disease initiation, progression, and metastasis, and have been associated with a worse prognosis in patients with gastric cancers [5].

Vascular endothelial growth factor (VEGF) is a signal protein produced by cells that stimulates vasculogenesis

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