Recombinant adenovirus-mediated overexpression of PTEN and KRT10 improves cisplatin resistance of ovarian cancer in vitro and in vivo

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ABSTRACT. Drug resistance is a major cause of treatment failure in ovarian cancer patients, and novel therapeutic strategies are urgently needed. Overexpression of phosphatase and tensin homolog (PTEN) has been shown to preserve the cisplatin-resistance of ovarian cancer cells, while cisplatin-induced keratin 10 (KRT10) overexpression mediates the resistance-reversing effect of PTEN. However, whether overexpression of PTEN or KRT10 can improve the cisplatin resistance of ovarian cancer in vivo has not been investigated. Therefore, we investigated the effects of adenovirus-mediated PTEN or KRT10 overexpression on the cisplatin resistance of ovarian cancer in vivo. Recombinant adenoviruses carrying the gene for PTEN or KRT10 were constructed. The effects of overexpression of PTEN and KRT10 on cisplatin resistance of ovarian cancer cells were examined using the 3(4,5-dimethylthiazol-2-yl)2,5-diphenyltetrazolium bromide (MTT) and TdT-mediated dUTP nick-end labeling (TUNEL) assays in vitro. Subcutaneously transplanted
nude mice, as a model of human ovarian cancer, were used to test the effects of PTEN and KRT10 on cisplatin resistance of ovarian cancer in vivo. The MTT assay showed that recombinant adenovirus-mediated overexpression of KRT10 and PTEN enhanced the proliferation inhibition effect of cisplatin on C13K cells. Recombinant adenovirus-mediated overexpression of KRT10 and PTEN also increased the cisplatin-induced apoptosis rate of C13K cells. Furthermore, recombinant adenovirus-mediated overexpression of KRT10 and PTEN enhanced the inhibitory effect of cisplatin on C13K xenograft tumor growth. Thus, recombinant adenovirus-mediated overexpression of KRT10 and PTEN may improve the cisplatin resistance of ovarian cancer in vitro and in vivo.

Key words: Cisplatin; Cisplatin-induced keratin 10; Ovarian cancer; Multi-Drug Resistance; Phosphatase and tensin homolog