

Up-regulation of p21^{WAF1/CIP1} by small activating RNA inhibits the *in vitro* and *in vivo* growth of pancreatic cancer cells

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ABSTRACT

Aims and background. To study the inhibitory effect of p21^{WAF1/CIP1} activation by saRNA on the growth of human pancreatic cancer cells PANC-1 *in vitro* and *in vivo*.

Methods and study design. A dsRNA (dsP21) targeting the p21^{WAF1/CIP1} gene promoter at position-322 relative to the transcription start site was transfected into PANC-1 cells. Expression of mRNA and protein was evaluated by semiquantitative RT-PCR and Western blotting. Proliferation of PANC-1 cells was measured by the MTT method, and the apoptosis rate was detected by flow cytometry. PANC-1 cells were transplanted subcutaneously in nude mice, and the inhibitory effect of dsP21 on tumor growth was observed.

Results. The introduction of dsP21 was shown to efficiently up-regulate expression of the p21^{WAF1/CIP1} gene in PANC-1 cells according to the results of RT-PCR and Western blotting ($P < 0.01$, compared with controls). The inhibitory effect on cell proliferation was confirmed by the MTT test ($P < 0.05$, compared with controls). The apoptosis rate of PANC-1 cells treated with dsP21 was significantly higher than that of the control cells ($P < 0.01$). Our experimental data showed that dsP21-mediated up-regulation of p21 expression exerted an apparent growth inhibitory effect on PANC-1 cells *in vivo*.

Conclusions. dsP21 targeting the p21^{WAF1/CIP1} gene promoter can specifically up-regulate expression of the p21^{WAF1/CIP1} gene in PANC-1 cells. It therefore has a substantially inhibitory effect on cell proliferation *in vitro* and *in vivo* and can be used as a new method and material for the gene therapy of pancreatic cancer.

Key words: apoptosis, p21, pancreatic cancer, small activating RNA.

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