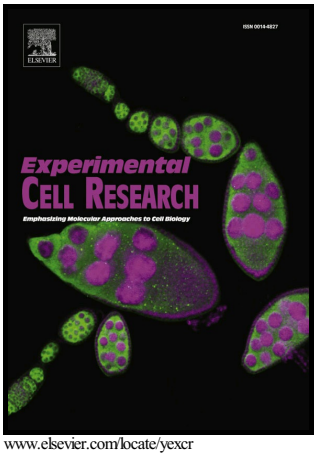

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Combination of DESI2 and endostatin gene therapy significantly improves antitumor efficacy by accumulating DNA lesions, inducing apoptosis and inhibiting angiogenesis

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ABSTRACT

DESI2 is a novel pro-apoptotic gene. We previously reported that DESI2 overexpression induces S phase arrest and apoptosis by activating checkpoint kinases. This work was to test whether the combination of endostatin, an endogenous antiangiogenic inhibitor, with DESI2 could improve the therapy efficacy *in vitro* and *in vivo*. The recombinant plasmid co-expressing DESI2 and endostatin was encapsulated with DOTAP/Cholesterol cationic liposome. Mice bearing CT26 colon carcinoma and LL2 lung cancer were treated with the DNA-liposome complex. We found that, *in vitro*, the combination of DESI2 and endostatin more efficiently inhibited proliferation of CT26, LL2, HCT116 and A549 cancer cells *via* apoptosis, as assessed by MTT assay, colony-formation assays, flow cytometric analysis, hoechst staining and activation of caspase-3, respectively. In addition, DESI2 overexpression caused up-regulation of RPS7, a substrate of DESI2 deubiquitination. Furthermore, siRNA targeting RPS7 partially abrogated, whereas RPS7 overexpression enhanced DESI2-induced inhibition of cell proliferation. Importantly, the combination also caused DNA lesions accumulation, which further promotes apoptosis. Mechanistic rationale suggested

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