Attenuated Salmonella typhimurium carrying TRAIL and VP3 genes inhibits the growth of gastric cancer cells in vitro and in vivo

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ABSTRACT

Background. Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand (TRAIL) and apoptin (VP3) of chicken anemia virus can selectively induce apoptosis in human tumor cell lines by two different pathways. Salmonella not only delivers functional genes to mammalian cells but also possesses antitumor activity and therefore could be adopted as a novel vector for anticancer therapy.

Materials and methods. TRAIL and VP3 genes were cloned into a pBudCE4.1 vector and delivered by attenuated Salmonella typhimurium into gastric cancer cells, and their expression and antitumor effects in nude mice were monitored by Western blot, fluorescence microscopy, MTT assay, TUNEL staining, and immunohistochemistry.

Results. pBud-VP3 and pBud-TRAIL-VP3 plasmids were constructed to express TRAIL and apoptin in gastric cancer cells, leading to inhibition of cancer cell proliferation after 48 hours (P <0.05). TRAIL and VP3 genes in pBudCE4.1 vector were also successfully delivered by attenuated S. typhimurium into gastric cancer cells in vivo, in which both TRAIL and apoptin were expressed. In vivo data indicated that S. typhimurium carrying pBud-TRAIL-VP3 induced significant cell growth inhibition and tumor regression (P <0.05). Moreover, expression of TRAIL and apoptin increased the expression of caspase-3 and caspase-9, resulting in enhanced apoptosis.

Conclusion. Delivery of TRAIL and VP3 genes by attenuated S. typhimurium can significantly inhibit the growth of gastric cancer cells in vitro and in vivo. Free full text available at www.tumorionline.it

Key words: gastric cancer, apoptosis, attenuated Salmonella typhimurium, TRAIL, VP3.

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