Investigation of the anti-cell proliferation effect of single vs dual gene therapy with apoptosis inducer genes on the growth of lung carcinoma cells

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Targeted gene delivery, high transfection efficiency, and safety concerns remain a challenge for effective cancer therapy by transgene. Although viral vectors are effective tools to deliver therapeutic genes to tumors, they are potentially pathogenic and are poorly targetable; this has led to the research of non-viral nanoparticle vectors. We have previously demonstrated that a pulmonary gene therapy with a single apoptosis inducer gene by a dimerized HIV-1 TAT peptide (dTAT) vector significantly attenuates the growth of Lewis lung carcinoma allograft in mouse lungs (Kawabata et al., 2012). The present study was aimed to evaluate the anti-cell proliferation effect of single vs dual gene therapy using A549 human lung carcinoma cells. In this study, three cell penetrating peptides (CPPs), dTAT, polylysine (K9), and polyethylenimine (PEI) nanoparticle (NP) vectors were used to transfect combinations of various apoptosis inducer genes, including angiotensin II type 2 receptor (AT2R), TRAIL, miR34a and tristetraprolin (TTP), 5 into A549 cells. A MTT assay was used to determine the cell proliferation over 72 hours. Among many single genes and two gene combinations, AT2R +TRAIL and AT2R+miR34a gene combinations showed time-dependent and stronger cell growth attenuation than single gene or other dual gene combinations. The miR34a and TTP single gene transfections showed stronger cell growth inhibition among four single genes. In conclusion, CPPs NP-based dual gene therapies with AT2R +TRAIL and AT2R+miR34a are more effective than single gene therapy. Therefore, it is suggested that CPPs NP dual gene therapy may be a good option for future cancer gene therapy.