Pro-apoptosis and anti-proliferation effects of a recombinant dominant-negative survivin-T34A in human cancer cells.

BACKGROUND: Survivin is an attractive target for anti-cancer drug development; however targeting it by small molecules or antibodies is difficult, as survivin is neither a kinase nor a cell surface protein. Protein transduction domain (PTD)-mediated macromolecular therapeutics provides an alternative avenue for targeting survivin.

MATERIALS AND METHODS: A plasmid expressing a dominant-negative survivin-T34A fused with the immunodeficiency virus protein transduction domain TAT was constructed. The fusion protein was expressed and purified from E. coli. The inhibition of proliferation and induction of apoptosis was tested in human lung carcinoma cell line A549 by directly adding survivin-T34A to the cell culture medium.

RESULTS: Recombinant survivin-T34A was efficiently expressed and purified by affinity chromatography. It induced cell apoptosis as demonstrated by induction of caspase 3 activation and higher percentage of Annexin V staining, and inhibited cell proliferation as determined by cell number counting.

CONCLUSION: This functional recombinant protein is promising for development of macromolecular therapeutics targeting survivin.