Original Article

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Targeted Nanoparticles Deliver siRNA to Melanoma

Yunching Chen, Surendar R Bathula, Qi Yang and Leaf Huang

Abstract

Melanoma is a severe skin cancer that often leads to death. To examine the potential of small interfering RNA (siRNA) therapy for melanoma, we have developed anisamide-targeted nanoparticles that can systemically deliver siRNA into the cytoplasm of B16F10 murine melanoma cells, which express the sigma receptor. A c-Myc siRNA delivered by the targeted nanoparticles effectively suppressed c-Myc expression in the tumor and partially inhibited tumor growth. More significant tumor growth inhibition was observed with nanoparticles composed of N,N-distearyl-N-methyl-N-2-(N′-arginyl) aminoethyl ammonium chloride (DSAA), a guanidinium-containing cationic lipid, than with a commonly used cationic lipid, 1,2-dioleoyl-3-trimethylammonium-propane (DOTAP). Three daily injections of c-Myc siRNA formulated in the targeted nanoparticles containing DSAA could impair tumor growth, and the ED_{50} of c-Myc siRNA was about 0.55 mg kg^{-1}. The targeted DSAA nanoparticles containing c-Myc siRNA sensitized B16F10 cells to paclitaxel (Taxol), resulting in a complete inhibition of tumor growth for 1 week. Treatments of c-Myc siRNA in the targeted nanoparticles containing DSAA also showed significant inhibition on the growth of MDA-MB-435 tumor. The enhanced anti-melanoma activity is probably related to the fact that DSAA, but not DOTAP, induced reactive oxygen species, triggered apoptosis, and downregulated antiapoptotic protein Bcl-2 in B16F10 melanoma cells. Thus, the targeted nanoparticles containing c-Myc siRNA may serve as an effective therapeutic agent for melanoma.