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Congress Abstract

Targeted Delivery of the CDC42 Inhibitor Casin to Colorectal Cancer Cells Using PLGA-PEG Nanoparticles Functionalized with Nucleolin-Binding Aptamers

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Introduction: Cdc42 is a small Rho GTPase that regulates various cellular functions controlling cell motility, shape, and growth through actin cytoskeleton dynamics. This protein is also known to be overexpressed in various diseases, particularly in cancer. Colorectal cancer is a common malignancy with a high mortality rate. Elevated Cdc42 expression is observed in colorectal cancer. Inhibition of Cdc42 can significantly slow the growth and metastasis of colorectal cancer but often causes severe side effects. To address this issue, PLGA-PEG nanoparticles functionalized with DNA aptamers were developed to selectively deliver the Cdc42 inhibitor CASIN to tumor cells by targeting nucleolin—a protein that is overexpressed in colorectal cancer.

Materials and Methods: The nucleolin-targeting aptamer AS1411 (5'-FAM–GGT GGT GGT GGT TGT GGT GGT GGT GG–3'-NH2) was synthesized as a 28-base single-stranded DNA oligonucleotide modified with a fluorescein label at the 5' end and an amine group at the 3' end. PLGA-PEG-NHS nanoparticles conjugated with the AS1411 aptamer were prepared using the nanoprecipitation method. Conjugation efficiency was assessed by DNA quantification, as well as by fluorescence microscopy and Raman spectroscopy. Binding affinity and specificity of aptamer-functionalized nanoparticles to nucleolin-positive cancer cells were confirmed by flow cytometry.

Results: AS1411-functionalized PLGA-PEG-NHS nanoparticles loaded with CASIN had an average size of approximately 129 nm (polydispersity index 0.259) and a zeta potential of –52.3 mV. Encapsulation efficiency was 38.1%, and drug loading content was 7.35%. CASIN release occurred in two phases: an initial burst release followed by a gradual release over 48 hours. In vitro, these nanoparticles significantly suppressed the growth of colorectal cancer cells (HT29, SW620, HCT116) and substantially reduced HT29 cell migration, while AS1411-modified nanoparticles without CASIN had minimal effects. Furthermore, the nanoparticles significantly reduced the migratory and invasive capacity of colorectal cancer cells.

Conclusion: Overall, this targeted nanoparticle system represents a promising strategy for improving the precision and efficacy of colorectal cancer treatment. This research was funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan (Grant No. AP26100973) and Nazarbayev University under Collaborative Research Project (CRP) No. 211123CRP1611.

Keywords: Colorectal Neoplasms; Molecular Targeted Therapy; Cdc42 GTP-Binding Protein; Nanoparticles; Polylactic-Co-Glycolic Acid (Copolymer); Nucleotide Aptamers