TARGETED DELIVERY OF CDC42 INHIBITOR CASIN TO COLORECTAL CANCER CELLS VIA NUCLEOLIN- BINDING APTAMER-FUNCTIONALIZED PLGA-PEG NANOPARTICLES

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Background: Blocking Cdc42 can significantly reduce colorectal cancer growth and metastasis, but it often causes serious side effects. To address this, PLGA-PEG nanoparticles coated with DNA aptamers were designed to selectively deliver the Cdc42 inhibitor CASIN to tumor cells by targeting nucleolin, a protein highly overexpressed in colorectal cancer.

Materials and methods: The nucleolin-targeting aptamer AS1411 (5′-FAM–GG TGG TGG TGG TTG TGG TGG TGG TGG–3′-NH2) was synthesized as a 28-base single-stranded DNA oligonucleotide, modified with a fluorescein label at the 5′ end and an amino group at the 3′ terminus. PLGA-PEG-NHS nanoparticles were produced via nanoprecipitation and then conjugated with the AS1411 aptamer. Conjugation efficiency was assessed by quantifying DNA content, as well as using fluorescence microscopy and Raman spectroscopy. The binding affinity and specificity of the aptamer-functionalized nanoparticles to nucleolin-positive cancer cells were validated through flow cytometry.

Results: The PLGA-PEG-NHS nanoparticles, functionalized with AS1411 and loaded with CASIN, had an average size of about 129 nm (PDI 0.259) and a zeta potential of –52.3 mV. The encapsulation efficiency was 38.1%, with a drug loading of 7.35%. CASIN release showed a two- phase pattern: an initial burst followed by sustained release over 48 hours. In vitro, these nanoparticles significantly suppressed the growth of colorectal cancer cells (HT29, SW620, HCT116) and strongly reduced HT29 cell migration, whereas AS1411-modified nanoparticles without CASIN had little effect.

Conclusion: Overall, this targeted nanoparticle system offers a promising strategy to enhance the precision and effectiveness of colorectal cancer therapy. This research has been funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan (Grant No. AP26100973) and Nazarbayev University, Collaborative Research Project (CRP) Grant No. 211123CRP1611.