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Oligonucleotide aptamers as novel cell-specific delivery agents for boron neutron capture therapy

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Abstract. Oligonucleotide aptamers seem to be promising delivery vehicles addressing boron compounds to tumour cells for boron neutron capture therapy (BNCT). Here, we report the first example of using 2'-F-RNA aptamer specific to human glioblastoma cells as a delivery agent for boron clusters, which provides cell internalisation sufficient for the BNCT model.

Key words: cell-specific aptamers, human glioblastoma cells, boron clusters, boron neutron capture therapy, cancer treatment, drug delivery.

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Boron neutron capture therapy (BNCT) represents a promising approach to treating malignant tumours, particularly glioblastoma: the most frequent and incurable brain tumour [1]. For effective BNCT, a boron-containing therapeutic agent should provide selective and effective accumulation of ^{10}B isotope inside target tumour cells, which are then destroyed after irradiation by an epithermal neutron beam. Nucleic acid aptamers are very promising candidates for selective delivery of ^{10}B compounds to tumour cells.

We employed a 2'-F-RNA aptamer specific to human glioblastoma U-87 MG cells as a delivery vehicle for a boron cluster covalently attached to the 5'-end of the aptamer through the click reaction between the 5'-alkyne-modified aptamer and azide-containing derivative of closo-dodecaborate [2]. Cluster-conjugated aptamer demonstrated effective and specific internalisation into U-87 MG cells and low toxicity. To establish the proof-of-principle of using boron-loaded aptamers for BNCT, the cells were incubated with the conjugate and irradiated on the Budker Institute of Nuclear Physics (BINP) neutron source. Then, cell proliferation was assessed through real-time cell monitoring and the clonogenic test. The results showed that boron-loaded aptamer specifically decreased the viability of U-87 MG cells to an extent comparable to that of ^{10}B-boronophenylalanine taken as a control.

Our study provides the first example of employing nucleic acid aptamer as a cell-specific boron carrier for BNCT. Taking into account their specificity, versatility, ease of chemical synthesis and large possibilities for high boron-loading, aptamers provide an up-and-coming basis for engineering novel BNCT agents.

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