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Targeted agents based on aptamers for the delivery of the 10B isotope in BNCT

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Glioblastomas are the most common type of malignant brain tumors, characterized by high aggressiveness and resistance to almost all currently existing methods of therapy. A promising approach to the treatment of such tumors is boron neutron capture therapy (BNCT), based on irradiation of tumor cells saturated with the boron-10 isotope with a neutron flux of a certain energy range. We have proposed a new strategy for boron isotope delivery based on the use of oligonucleotide aptamers of structured synthetic DNA and RNA fragments capable of selectively binding and penetrating tumor cells. A quantitative assessment of the level of boron achieved in tumor cells upon specific delivery in the form of a conjugate with the 2'-F-RNA aptamer was carried out [1]. For this purpose, two independent methods were used: quantitative real-time RT-PCR and inductively coupled plasma atomic emission spectrometry. The results obtained by both methods are in good agreement with each other. Aptamer-mediated delivery achieves intracellular levels of boron that exceed those required for effective BNCT (10^9 atoms/cell) [2]. The biodistribution of boron-containing GL44 2'-F-RNA aptamer conjugates was studied in SCID mice bearing subcutaneous U-87 MG human glioblastoma xenografts *in vivo*. For this purpose, methods of intravital fluorescence imaging and atomic emission spectroscopy were used. Fluorescence imaging did not reveal significant differences between the experimental and control groups. However, studying the distribution of boron in individual organs of model animals revealed higher levels of boron in the tumor xenograft. The results obtained on inhibition of tumor growth, survival and tumor node weight allow us to preliminary evaluate the effect of the aptamer conjugate GL44-5B12 as specific. The results obtained allow us to draw a preliminary conclusion about the specific effect of the boron-containing aptamer conjugate on the in vivo tumor model. Undoubtedly, to confirm this effect, study it in detail and select the optimal dosage and irradiation regimen, improving the pharmacokinetic characteristics of aptamer conjugates, further additional experiments will be required, which will be the development of this work. We have demonstrated the low toxicity of 2'-F-RNA conjugates with closo-dodecaborate, the specificity of their interaction with tumor cells *in vitro* and *in vivo*, the ability to deliver the amount of boron required for BNCT into cells, as well as the positive results of model experiments on BNCT confirm the promise of such studies.

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References:

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