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Targeted delivery of chemotherapeutic agents to brain tumors

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Human glioblastoma multiforme is the most frequent and aggressive type of brain tumors. The purpose of this study was to design cisplatin-loaded nanogels conjugated with monoclonal antibodies to membrane protein connexin 43 (Cx43) or to brain-specific anion transporter type 1 (BSAT1) for treatment of glioma 101/8 and glioma C6 *in vivo*.

Nanogels were loaded with anticancer drug cisplatin (CDDP) and conjugated to mAbs (Cx43 or BSAT1). Glioma C6 cells were used to evaluate the cellular uptake of cisplatin-loaded nanogels as well as their cytotoxicity. Antitumor effect of formulations (CDDP, nanogel/CDDP, IgG-nanogel/CDDP, mAb-nanogels/CDDP and 5% dextrose) on glioma 101/8 and glioma C6 was evaluated by measurement of tumor volume using 7T MR-tomograph (ClinScan, Bruker).

The mAb-conjugated nanogels represented stable negatively charged particles (about 120 nm) with high loading capacity (up to 35 % w/w). *In vivo* analysis in tumor-bearing rats indicated significantly reduced tumor burden and increased lifespan with cisplatin loaded into specific targeted-nanogels compared to other formulations. Free CDDP showed a similar antitumor activity in comparison with mAbCx43-nanogel/CDDP or mAbBSAT1-nanogel/CDDP, however revealed profound loss of body weight (systemic toxicity) and neurotoxicity (dilatation of the subarachnoid space and ventricle of brain). The mAb to BSAT1 as a targeting moiety was more efficient than mAbCx43.

The drug-loaded targeted nanogels exhibited enhanced tumor growth inhibition, increase in the lifespan and no loss of the body weight in comparison with other investigated formulations. These nanogels could be used as a platform for targeted delivery of chemotherapeutic agents in Cx43- or BSAT1-positive high grade gliomas.

Biography

Dr. Nukolova has completed her Ph.D. in polymer chemistry from Moscow State University (Adviser: Prof. Kabanov, UNMC). Following a fellowship at University of Nebraska Medical Center (UNMC), Dr. Nukolova joined the faculty at the Serbsky National Research Center for Social and Forensic Psychiatry in Moscow as a Senior Staff Scientist. Her major interest is development of new approaches for diagnosis and treatment of cancer.

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