Секция «Вирусология»

Development of new recombinant Oncolytic poliovirus for glioblastoma treatment.

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Glioblastoma multiforme is the most common and malignant form of brain neoplasms and aggressive primary central nervous system (CNS) malignancy. That is why it is necessary to develop new strategies for its treatment [1]. Currently, the FDA has approved the only strain for cancer virotherapy - T-Vec, HSV-1 derived oncolytic virus [3]. However, therapy with oncolytic viruses, originally developed for the treatment of intraparenchymal solid tumors, is also promising for glioblastoma. The pathogenicity of wild-type poliovirus in neuronal cells precludes it from therapeutic use. To overcome natural neuropathogenicity, a modified vaccine strain of poliovirus type 1 (Sabin) was created, in which the internal ribosome entry site (IRES) was replaced with the IRES of human rhinovirus type 2. Due to this modification, the virus has lost its ability to cause disease in laboratory animals, while retaining cytopathogenicity against malignant glioblastoma cells [2]. This strain (PVS-RIPO) is in the final stages of clinical trials. We have developed a recombinant strain based on the vaccine strain of poliovirus type 3, the IRES of which was replaced by the IRES of a non-pathogenic strain of living enterovirus vaccine LEV14 [3], for which high specific cytotoxicity against tumor cells was shown. The assessment of tropism and oncolytic properties has shown that this virus is able to effectively infect and lyse cells of glioblastoma cultures (model lines DBTRG, U251-MG, as well as primary cell lines), while it did not demonstrate cytotoxicity against human embryonic fibroblasts and embryonic astrocytes, demonstrating different tropism in comparison with vaccine poliovirus type 3. Additionally hepatocellular carcinoma cell line (HepG2), hepatoma-derived HuH-7 cell line and normal hepatocytes (HepaRG) were tested for its sensitivity to new strain. While it has restricted replication in normal hepatocytes, it could replicate efficiently in HepG2 and HuH-7, giving hope for the effectiveness of its use in malignant liver tumors. This virus was named Russo, it successfully passed safety tests on preclinical studies. The work was supported by the Russian Science Foundation (grant no. 20-75-10157).

References

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