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Attenuated oncolytic vaccinia virus for treatment of glioblastoma

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MicroRNAs play a crucial role in gene regulation, controlling key processes of tumor growth and metastasis. They are widely used as prognostic markers of cancerous tumors, and their selective expression in tumor cells makes them a useful tool for targeted viral therapy. miR-21 is one of the most studied oncogenic microRNAs and is overexpressed in glioblastomas (GB). GBs often exhibit defective interferon signaling. The LIVP strain of vaccinia virus (VV) demonstrates differential oncolytic activity in these tumors, suggesting a potential mechanism for targeted therapeutic intervention. To investigate this further, we engineered a recombinant VV strain incorporating a miR-21-5p binding site upstream of an open reading frame encoding human interferon-α (IFNα) and the fluorescent protein tagRFP. Experimental results indicate that IFNα expression does not significantly compromise the viral ability to replicate in tumor cells or prevent the formation of infectious foci. In tumor cells with high miR-21 expression, the transcript with binding site is cleaved, preventing IFNα and tagRFP expression. Conversely, in normal cells with low miR-21 levels, IFNα is expressed at high levels, triggering an antiviral response that inhibits viral replication and protects the surrounding tissue. The expression level of miR-21 was assessed in a panel of primary and model GB cell lines, and viral kinetics were analysed. Our results confirmed that microRNA interference efficiently regulates IFNα/RFP expression in the oncolytic virus, supporting the concept of a microRNA-attenuated viral design. This work was supported by the Russian Science Foundation (grant no. 23-74-10102).

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Anticancer activity of pleurocidin family NRC-03 peptide against cervical cancer cells

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NRC-03 is a 26-residue cationic antimicrobial peptide belonging to the pleurocidin family, derived from skin mucous secretions of winter flounder (*Pleuronectes americanus*). Although pleurocidin-like peptides were originally demonstrated as broad-spectrum antimicrobials, many studies reveal their potent cytotoxic properties against cancer cells, including breast cancer or leukemia cells. The cationic structure of NRC-03 allows it to specifically target cancer cells that have negative charges leading to the rupture of their membranes and ultimately causing cell death. Importantly, NRC-03 exhibits lower toxicity towards normal cells. To date, the ability of NRC-03 to inhibit the growth of cervical cancer cells has not yet been studied. Moreover, the molecular mechanisms governing the NRC-03-induced death of cervical cancer cells remain unknown. This study focuses on elucidating the possibility of employing the NRC-03 peptide as a therapeutic agent against cervical cancer cells and decoding the mechanism of cytotoxicity of this peptide. To achieve that, the viability of cervical cancer HeLa cells, their morphology as well as their proliferation capability was explored using colorimetric and microscopic methods. The induction of apoptosis and other cell death mechanisms was investigated using flow cytometry, fluorescence microscopy and gene profiling. Biocompatibility of the peptide was assessed using a vaginal epithelial cell line (VK2/E6E7) and human erythrocytes. We demonstrated that the NRC-03 peptide decreases significantly the viability of cervical cancer cells while offering the appropriate biocompatibility. Our results strongly encourage further studies on the utility of NRC-03 peptide as an anticancer molecule in the treatment of cervical cancer. Funding: Financial support was received from the Medical University of Bialystok (B.SUB.25.407 to EP).

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Cytotoxic effects of polyphenolic cocktail (PFK5120), salicylic acid and indole-3-carbinol combinations on gastric adenocarcinoma cell line

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Cancer is the leading cause of morbidity and mortality worldwide. Among all cancer types, gastric cancer is one of the most lethal cancer due to its high incidence, poor prognosis and low survival rates. Studies have revealed the anticancer properties of plant secondary metabolites via apoptosis inducing effects. Changes in the expression levels of BAX, BCL2 and BAD genes, which have key roles in mitochondrial apoptosis, have been shown in previous studies. In this research, AGS cell line, and HUVEC cell line were treated with PFK5120, indole-3-carbinol (I3C), salicylic acid (SA) individually and combined forms at certain doses and times. Cytotoxicity analysis was performed by WST-8 method, and real-time PCR method was used to indicate the changes in the expression levels of BAX, BCL2, and BAD genes. According to WST-8 analysis, at 48 h, PFK5120 exhibited a strong cytotoxic effect on AGS cells across all doses, I3C showed a strong cytotoxic effect at 15 μg/mL dose, and SA had cytotoxic effects at doses of 60 μg/mL and 125 μg/mL ($p < 0.0001$ for each). On the other hand, WST-8 analysis revealed that the treatment with combinations showed more cytotoxic effect on cancer cells, and the combined treatment caused a lower cytotoxic effect on HUVEC control cells. Individual treatments caused an upregulation in BAX and BAD expressions and a downregulation in BCL2 expression. Also, while the combination of PFK5120/I3C shows the similar results as individual applications, PFK5120/I3C/SA application demonstrates an opposite result. In this context, the effect of the combined use of I3C and SA on apoptosis mechanisms should be investigated in more detail. In particular, future studies should clarify whether these compounds exert their antiproliferative effects through different signaling pathways. The findings obtained provide significant contributions to the evaluation of plant-derived secondary metabolites as potential adjuvant agents in cancer treatment.

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