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Apoptin enhances the oncolytic properties of vaccinia virus and modifies mechanisms of tumor regression by virus

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Some effective oncolytic viral recombinant strains engineered on the base of adeno-, herpes and vaccinia (VACV) viruses have been recently reported. We constructed apoptin-producing recombinant VACV based on L-IVP vaccinia strain in which the apoptin gene was inserted instead of deleted C11R-gene encoding viral growth factor. The obtained recombinant VVdGF-ApoS24/2 effectively produced apoptin in the infected cells, and demonstrated a significantly greater lytic activity on cancer cell lines (A549, A431, U87MG, RD and MCF7) as compared with parental L-IVP. The oncolytic effect was examined by virological, light and electron microscopy methods. Regression of the tumor after L-IVP strain injection was accompanied with formation of cavities filled with cell debris and liquid, while apoptin-producing strain caused shrinkage of the tumor. Surprisingly, the immunohistochemical analysis has revealed that unlike the previously described preferentially nuclear localization of apoptin in cancer cells, the apoptin produced by the VVdGF-ApoS24/2 is localized to the cytoplasm. We suggest that apoptin expressed by VVdGF-ApoS24/2 does not induce a typical apoptosis, but rather modified the virus-induced cell death in such a way that the tumors shrink without the excessive formation of cell debris and exudates.

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