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The effect of DNA synthesis inhibitor on DNA damage induction in melanoma cells after exposure to protons

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Increasing the radiosensitivity of normal and tumor cells is one of the priority aims of modern radiobiology. The agents that modify the yield of DNA double-strand breaks (DSBs) which are lethal to cells are of particular interest. We have previously shown that under the influence of DNA repair inhibitors - 1-β-D-arabinofuranosyl cytosine (AraC) and hydroxyurea (HU) the DNA DSBs yield on cells of various types increases under the action of ionizing radiation. The mechanism of this process is based on the long-term non-reparable DNA single-strand breaks (SSBs) conversion into enzymatic DSBs.

The main aim of this research was to elucidate the molecular and cellular effects of the proton action on the murine melanoma B16 cells under the influence of AraC and HU. The samples for analysis were taken after 2 and 10 days of melanoma cells transplantation into the animals and irradiation with protons at a dose of 10 Gy. Two modifications of quick and highly sensitive comet assay were carried out: in neutral conditions to detect DNA double-strand breaks, and in alkaline conditions to detect DNA single-strand breaks. It was found that the amount of DNA SSBs and DSBs significantly increases under the influence of AraC. This difference persists in the post-radiation period up to 10 days.

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