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Induction of DNA damage in neuronal cells of mice under the influence of repair inhibitors under the action of gamma-rays in vivo

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The search for approaches aimed at changing the sensitivity of cells to the action of ionizing radiation is one of the priority tasks of radiobiology. Studies of the modifying action of agents that affect the processes of DNA damage repair in the cells of the central nervous system (CNS) appear to be promising. In this regard, agents that influence the yield of DNA double-strand breaks (DSB) are of interest. We have previously shown that under the influence of inhibitors of DNA repair - 1-β-D-arabinofuranosyl cytosine (AraC) and hydroxyurea (HU), the yield of DNA DSB increases upon γ-irradiation of cells of various types in vitro. The mechanism of this process is based on the transformation of long-term non-repairable single-strand breaks (SSB) of DNA into enzymatic DSB. In this case, the magnitude of the modifying effect of these agents depends on the quality of the radiation.

In this work, we performed a comparative analysis of the induction and repair of DNA SSB and DSB in neuronal cells of mice (hippocampus and cerebellum) under γ-irradiation after intraperitoneal administration of AraC and AraC/HU combination in vivo.

DNA comet assay method was used to study the regularities in the formation of DNA SSB and DSB in cells from hippocampus and cerebellum of mice under the action of γ-radiation in vivo, under the influence of AraC and HU. It was found that for all types of cells used, there is a linear character in the yield of DNA lesions. It has been shown that the amount of DNA SSBs and DSBs formed during irradiation under the influence of AraC significantly increases. An additional increase in the yield of DNA SSBs and DSBs is observed under the combined action of AraC and HU.

The kinetics of DNA SSB and DSB repair was studied under the influence of radio modifiers. It has been shown that the kinetics of DNA SSB and DSB repair both in hippocampal and cerebellar cells is complex. Up to 4 hours post-irradiation, an increase in the yield of DSB is observed to the maximum values, after which their decrease is observed for all types of cells. Although the kinetics of SSB repair, as well as for DSB, exhibits a biphasic character, differences are also observed depending on the cells. Thus, for cerebellar cells, the maximum of SSB shifts by 2h post-irradiation; for hippocampal cells, the maximum of SSB are similar with the maximum observed for DSB and falls on 4h post-irradiation. Under the conditions of the influence of AraC alone and the combined influence of AraC/HU, an increase in the total amount of damage is observed during the entire post-irradiation period observed in the experiment.

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