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Influence of high-energy proton and gamma-radiation on DNA structure in solution

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The use of a specific technique and type of radiation in radiotherapy of tumors is determined by various factors: the localization of the tumor in the body, its oxygenation, the stage of the disease, the availability of the technique for the patient, etc. The study of damage in the DNA structure under the influence of different types of radiation and with varying irradiation conditions provide important information for improving the methods of radiation therapy. This work compares the damage in the DNA structure under the action of ^{60}Co γ-radiation (used in the gamma knife therapeutic device) and 1 GeV protons (at synchrocyclotron of the St. Petersburg Institute of Nuclear Physics Research Center "Kurchatov Institute" SC-1000, since 1975 there has been a medical center for stereotactic proton therapy). These two types of radiation have the same value of LET = 0.3 keV/μm.

Disturbances in the DNA structure were studied by spectrophotometric melting. The parameters of the helix-coil transition in the irradiated macromolecule are influenced by various types of radiation damage. Single- and double-strand breaks, destruction, modification, and release of nucleobases lead to destabilization of the secondary structure and lower the melting temperature of DNA (Tm), while interstrand cross-links increase Tm [1].

Melting curves of DNA irradiated with doses of 0-100 Gy were obtained at ionic strengths of solutions of 5 mM and 150 mM $NaCl$, as well as at a total ionic strength of 5 mM = 3 mM Na^+ + 2 mM Mg^{2+}. The absorption spectra of DNA solutions were measured at 25^oC, 95^oC, as well as after melting and rapid (within 10 min) cooling to 25^oC. From these data, the helix-coil transition interval, Tm, the DNA molar extinction coefficient, the hyperchromic effect, and the degree of DNA renaturation after melting upon rapid cooling were determined. Proton and γ-irradiation cause a broadening of the melting interval, which indicates an increase in the heterogeneity of the DNA structure, i.e. the appearance in the DNA chain of regions that differ sufficiently in thermal stability. For DNA irradiated in 150 mM $NaCl$ solutions with proton and γ-radiation, several maxima are observed in the differential melting curves. Under these conditions, it is possible to assume the formation of cross-links (both between two complementary strands and between DNA regions distant along the chain) as a result of irradiation. In 0.15M $NaCl$ solutions, the secondary structure of DNA is more resistant to radiation than in 5mM $NaCl$ solutions. It was found that proton irradiation causes a smaller drop in DNA Tm than γ-irradiation in a 0.15M $NaCl$ solution at doses of 0–100 Gy and in a 5 mM $NaCl$ solution at doses of 70-100 Gy. For the DNA irradiated with protons at doses of 10 and 20 Gy, an abnormally large hyperchromic effect was recorded, exceeding the value measured for native DNA. The data obtained allow us to conclude that under proton irradiation, clustered damage are formed in the DNA structure – slowly repairable or unrepairable sites, while under γ-irradiation, isolated DNA lesions appear, which can be quickly and efficiently repaired in the cell [2]. Thus, irradiation with high-energy protons has a greater lethal effect on the cell than γ-irradiation.

References

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