CHROMATIN STRUCTURE IN THE TUMOR CELLS WITH RADIORESISTANT PHENOTYPE

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The use of radiation therapy in the treatment of malignant neoplasms has long faced the problem of the emergence of tumor cells with radioresistant phenotype [1]. The mechanisms of radioresistance are commonly associated with the activation of signaling pathways and molecular cascades, including repair factors and inhibition of apoptosis pathways [2]. However, such changes in the cell metabolism and transcriptional patterns appear unlikely to be induced on a pure genetic level, but rather seem to involve epigenetic mechanisms that may in turn rely on the changes in the chromatin arrangement in the cell nucleus [3]. Changes in the density of chromatin packing could have additional effects on radioresistance by increasing the availability of the damaged DNA for repair and decreasing the stacking density and therefore the likelihood of the formation of intra- and inter-strand cross-links. Using cytometry, confocal microscopy, and small angle scattering we have investigated the structural properties of chromatin isolated by the standard procedure [4] from cells exposed to γ-radiation. including radioresistant phenotype of the Ehrlich's adenocarcinoma cells (transplantable after irradiation of 40 Gy, compared to 20 Gy in the initial cell population) that was obtained in a series of tumor irradiations. The results of SANS and SAXS measurements show that in contrast with the normal rat lymphosytes, on the scales 10-100 nm the chromatin arrangement of Ehrlich's adenocarcinoma cells was only slightly affected by radiation doses up to 2 kGy, while most of the changes in chromatin in response to radiation were observed on the scales ~2-3 nm that corresponds to the size of the DNA double helix. A comparative analysis of the data obtained by various methods in conjunction with data on the radioresistant properties of the studied cell population indicate that chromatin structural organization exhibits different behavior in response to radiation damage in the cells with different radiosensitivity.

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