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A NEW HAFNIUM-BASED RADIOSENSITIZER PROVIDE SELECTIVE X-RAY INDUCED CYTOTOXICITY *IN VITRO*

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Radiation therapy still remains the «gold standard» in cancer treatment. Lung and breast cancer are the most common types of cancer cases. One of the most promising approaches to increasing the efficiency of tumor radiation therapy is the use of radiosensitizers. This approach allows achieving a therapeutic effect at lower radiation doses, thereby reducing radiation exposure to healthy tissues.

One of the promising candidates as a nanodispersed radiosensitizer is nanocrystalline hafnium oxide. Hafnium is a heavy Z-element which it is able to efficiently absorb and re-emit ionizing radiation energy. Here we reported about new scheme of hafnium-containing nanocomposite synthesis with their additional functionalization using flavin mononucleotide [1]. This technique makes it possible to obtain a stable sol of a hafnium-containing nanocomposite with ultra-small particles (hydrodynamic radius of 3-4 nm) and high colloidal stability. The radiosensitization effects of hafnium-containing nanocomposite were investigated on normal and cancer cell lines using MTT assay under X-ray exposure (15 Gy). The intracellular localization analysis of nanocomposite showed that in A431 and MCF-7 cells effectively uptake the nanocomposite within an hour, while mouse fibroblasts and mesenchymal stem cells lower efficiency of nanocomposite endocytosis in high concentration (0.2 mg/ml). Moreover, after 12 hours of incubation, the maximum of nanocomposite cellular accumulation was observer predominantly in lysosomes.

The results of radiosensitization of hafnium-oxide nanocomposite via MTT assay demonstrated a strong dose-dependent decrease in the viability of tumor cell lines (A431 and MCF-7) after irradiation at a dose of 15 Gy with the nanocomposite at 0.3 mg/ml. At the same time, these cytotoxicity effects of hafnium-containig nanocomposite were significantly lower in relation to normal cells (L929 and DPSc).

Thus, according to our results, a hafnium-containing nanocomposite functionalized with a flavin mononucleotide can be considered as a promising radiosensitizer agent for X-ray radiation therapy.

References

[1] Bartmann L., Schumacher D., Saskia von Stillfried et al. *Front. Pharmacol.,* **2019**, 1467-1483

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