# Radioresistance of breast cancer stem cells after single-dose and fractionated γ-radiation exposure and radiosensitizing effect of dimeric bisbenzimidazoles *in vitro*

**Matchuk Olga N, Churyukina K A, Zhuze A L** and **Zamulaeva I A**
A Tsyb Medical Radiological Research Center, Russia

Numerous studies have proven the high resistance of cancer stem cells (CSCs) to a single-dose low-LET ionizing radiation exposure in vitro. However, the patterns and mechanisms of fractionated radiation effects on this population of cells have not been studied enough. The aim of the study was to elucidate effects of single-dose and fractionated γ-radiation exposure on CSCs of breast adenocarcinoma line MCF-7 and reveal means for CSC radio sensitization by inhibition of DNA damage repair. CSCs were isolated as $CD44^{+}CD24^{low/-}$ cells or side population (SP) by flow cytometry. Both methods were used to show a statistically significant increase in the relative and absolute number of CSCs both after single-dose and fractionated irradiation at doses of 4 Gy and more. These data were the basis for further work in order to reduce the resistance of CSCs in the range of 4-6 Gy. Synthetic dimeric bisbenzimidazoles – DB(n) that specifically bind to DNA A-T enriched sequences and inhibit a number of enzymes involved in chromatin remodeling and repair of DNA damages were synthesized. In our experiments length of oligomethylene linker (n) between two bisbenzimidazole blocks ranged from 1 to 11. DB (5) and DB (7) in combination with irradiation significantly reduced the proportion and clonogenic ability of CSCs compared with those after radiation exposure ($p<0.05$). The coefficients of the synergistic effect of these compounds and radiation on CSC clonogenicity were 1.3 for DB (5) and 1.2 for DB (7). Thus, the results showed that DB (5) and DB (7) could be used to develop anticancer drugs for elimination of CSCs and increase the effectiveness of cancer patient radiotherapy.

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## Speaker Biography

Matchuk Olga N has completed her PhD from A. Tsyb Medical Radiological Research Center, Russia in 2016. She is senior researcher of Laboratory of Radiation Biochemistry of Medical Radiological Research Center. She has over 50 publications (in English and Russian) that have been cited over 90 times, and her publication H-index (Scopus) is 4.

**e**: matchyk@mail.ru

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