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Abstract of the dissertation entitled:
Factors modulating cellular response induced by ionizing radiation

Ionizing radiation could ionize the medium through which it passes. Penetrating a cell, ionizing radiation can lead to damage to organelles. Cells and living organisms are characterized by different sensitivity to radiation. There are many physical, chemical, or biological factors influencing the radiosensitivity of cells, tissues, and organs. In the present study, the factors analyzed to modulate the gamma radiation-induced cellular response were temperature, low adaptive dose, and intracellular and intercellular differentiation in U2OS cells.

In studies of DNA damage response mechanisms, to inhibit DNA repair during radiation exposure, irradiation of cells on melting ice is a frequently used method. It is assumed that the effect of cooling cells is a reversible inhibition of DNA repair. However, studies have shown that hypothermia during irradiation not only inhibits DNA repair, but also modulates the DNA damage response to radiation. The aim of this part of the dissertation was to study the effect of low temperature, during exposure of U2OS cells to ionizing radiation. The effects of hypothermia on the formation and decay of NBS1, γH2AX and 53BP1 repair foci, on cell cycle progression, cell survival and inappropriate repair of DNA damage were investigated by analyzing the frequency of micronuclei. The results from this part of the study showed that the cooling of cells on melting ice probably led to a decrease in the activity of antioxidant systems or disruption of mitochondrial membrane integrity, resulting in the release of reactive oxygen species. Therefore, the increased levels of γH2AX and 53BP1 foci may be an adaptive response to low temperature-induced oxidative stress. The observed increased frequency of foci was due to an over-reaction of the DDR after exposure of U2OS cells to hypothermia. Results from the micronuclei assay showed increased levels of misrepair damage, and this result reflected an impaired G_2 phase block. The low temperature effect is limited only to the late phase of the cell cycle and does not modify the survival of U2OS cells.

In the part of the paper concerning the analysis of intra- and intercellular variation in sensitivity to radiation-induced DNA damage, the results showed that environmental factors present during cell culture *in vitro*, affect the radiosensitivity of U2OS cells at the level of 53BP1 foci. The increased number of foci in binucleated cells compared to mononucleated cells indicated that the so-called "bystander effect" may have occurred between the binucleated nuclei, whereby signals were emitted from the irradiated nucleus to amplify the level of damage.

Adaptation to the environment is essential for the survival and proper functioning of cells, tissues, and the entire organism. Due to natural processes, environmental pollution and occupational activity, people are constantly exposed to low doses of genotoxic agents. Exposure to low doses of ionizing radiation is a common phenomenon, for example, through medical diagnostics, occupational or environmental exposure. The radiation-induced adaptive response is a phenomenon that has been known for decades. Recent studies have shown that cells that were not direct targets of radiation were able to adapt if they had previously been in contact with cells that had been adapted with an adaptive dose. In vitro experiments, on the other hand,

face the problem of radiation sources with much higher dose rate than those that occur naturally in nature. A consequence of this problem is that the duration of radiation exposure is likely to be too short and perhaps insufficient to induce full cellular adaptation. Another interesting aspect is the role of ATM kinase signaling in the cell's response to DNA damage in the process of adaptation to very low doses of ionizing radiation. The results obtained in this part of the study showed that cells exposed to low doses of adaptation for 192 hours, induced activation of the cell's repair systems, which was noted as a constant level of 53BP1 repair foci in all the fixation times studied. Another aspect was the role of ATM kinase in the DNA damage response. Cells exposed to an adaptive dose, during ATM inhibition, were able to switch on an alternative sensor capable of recognizing unrepaired DNA damage.

The results demonstrate the complexity of radiation effects and expand knowledge of the biological effects of radiation and the factors that modulate the cellular response.

19.09.2022 Magdalena Płódowska

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