The Effect of PJ-34 and Ionizing Radiation on Viability of MDA-MB-231 Human Triple Negative Breast Cancer Cell Line

6th Kaunas / Lithuania International
Hematology / Oncology Colloquium
28 May 2021

Agnė Bartnykaitė[1], Rasa Ugenskienė[1,2], Arturas Inčiūra[3], Elona Juozaitytė[3]

[1] Oncology Research Laboratory, Oncology Institute, Lithuanian University of Health Sciences, [2] Department of Genetics and Molecular Medicine, Lithuanian University of Health Sciences, [3] Oncology Institute, Lithuanian University of Health Sciences

Objective

Radiation therapy plays an important role in the treatment of breast cancer but sometimes its effect is limited by the radioresistance of cancer cells. Poly (ADP-ribose) polymerase (PARP) is a family of proteins involved in many cellular processes, especially, DNA repair. Various PARP inhibitors have been demonstrated to exhibit anti-cancer activity as a single agents and in combination with chemotherapeutic agents or radiation therapy. PJ-34, one of the PARP inhibitors, has been shown to sensitize other types of tumor to chemotherapy and radiotherapy. However, the analysis has never been done on MDA-MB-231 human triple negative breast cancer cells in combination with ionizing radiation. Thus, the aim of the study was to analyze the combined effect of PJ-34 and ionizing radiation on proliferation of MDA-MB-231 cells.

Methods

Human triple negative breast cancer cell line MDA-MB-231 was used for the study. Cells were grown as monolayers in Dulbecco's Modified Eagle's medium (DMEM; Sigma-Aldrich) supplemented with 10% fetal bovine serum (Gibco), 100 U/mL penicillin with 100 µg/mL streptomycin (Gibco) and 2 mM L-glutamine (Gibco) at 37ºC in humidified 5% CO_2.

PJ-34 solution was purchased from SigmaAldrich, and frozen at −80ºC in small quantities to prevent freeze-thaw cycles. Working solutions were prepared before each experiment.

Cells were treated with different concentrations of PJ-34 one hour before irradiation. Cell irradiations were performed with the single dose of 1, 2, and 4 Gy, using a medical Clinac 2100C/D linear accelerator. Cells were irradiated with the drug present in the medium, and were immediately returned to the incubator.

The effect on MDA-MB-231 breast cancer cells was evaluated by MTT (3-(4,5-Dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide) cell proliferation assay 71 hours after the irradiation.

Results

We examined the effect of PARP inhibitor PJ-34 and ionizing radiation on proliferation of MDA-MB-231 triple negative breast cancer cells using MTT assay (Fig. 1).

The results demonstrated that PJ-34 alone affects cells viability in a dose-dependent manner and the significant decrease was observed after the treatment with concentrations of 10 and 30 µM.

Ionizing radiation alone also significantly reduced cell viability, however, the results following the radiation with 1 and 2 Gy were very similar.

For the combined effect analysis, cells were treated with PJ-34 and exposed to a single radiation dose of 1, 2 or 4 Gy. MTT assay revealed that the combination therapy of 10 and 30 µM PJ-34 and radiation (1, 2 and 4 Gy) produced a significant decrease in MDA-MB-231 viability in a dose-dependent manner in comparison to radiation alone.

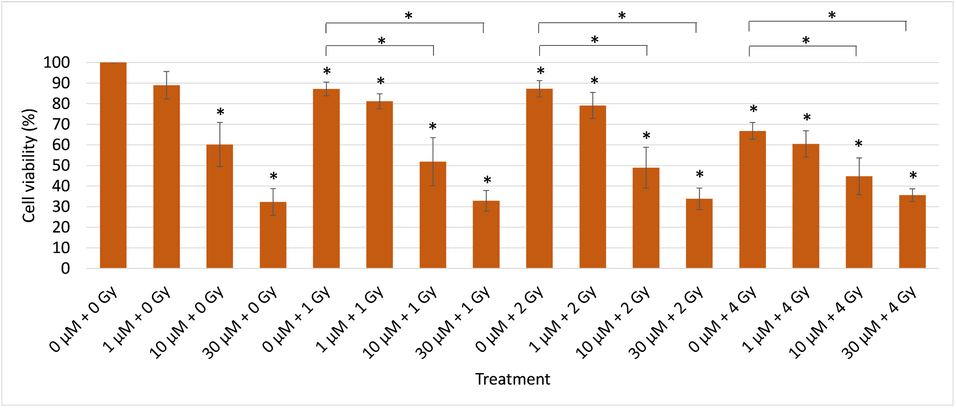

*Figure 1. MDA-MB-231 cells viability determined by MTT assay 71 hours after the irradiation. Data are shown as % of untreated control group (0 µM + 0 Gy). All error bars represent the SD. (*) means difference compared with untreated group, *p < 0.05.*

Conclusions

Overall, the current findings suggest that PJ-34 improved the response to ionizing radiation on MDA-MB-231 cells by increasing the inhibition of cell proliferation. It can be concluded that PJ-34 acts as a radiosensitizer and requires further study to elucidate the molecular mechanisms responsible for the sensitizing effect.

ACKNOWLEDGMENTS. This work was funded by the European Union's Horizon 2020 research and innovation programme under grant agreement no 730983 (INSPIRE).

Key words

breast cancer, MDA-MB-231, PJ-34, ionizing radiation