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IONIZING RADIATION INDUCES MONO- AND MULTINUCLEATED GIANT CANCER CELLS IN A DOSE-DEPENDENT MANNER IN HELA CELLS *

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Abstract

We investigated the effect of ionizing radiation on HeLa cancer cell. Our results show that ionizing radiation induces dose-dependent formation of polyploid giant tumour cells, with higher doses (8 and 12 Gy) leading to a greater number of these cells, while lower doses were insufficient for their formation.

Radiotherapy relies on ionizing radiation to induce DNA damage in cancer cells, ultimately leading to cell death. However, this death is not always immediate and may result in the survival of cancer cell subpopulations with altered properties. One such outcome is the formation of Mono- and Multinucleated Giant Cancer Cells (MGCCs)/Polyploid giant cancer cells (PGCCs), genetically unstable cells that can arise from failed cytokinesis, cellular fusion or aberrant cell division processes. These cells are increasingly recognized for their role in therapy resistance, dormancy, tumour repopulation, and metastasis.

Our study aims to characterize the formation of MGCCs following ionizing radiation in cancer cell lines, starting with HeLa cells. The experiments were conducted using the Novalis TX electron accelerator, delivering radiation at a dose rate of 600 Gy/hour. The lethal dose 50 (LD50) for HeLa cells was determined to be 6 Gy and used to guide experimental dose selection.

HeLa cells were irradiated with 4 Gy, 8 Gy, and 12 Gy, and giant cell formation was monitored over a 5-day period. By day 3, 8 Gy irradiation induced a prominent population of MGCCs, including both mononuclear and multinucleated forms, making it an optimal dose for yielding these therapy-resistant cells. By day 5, a noticeable increase in giant cell percentage was observed in the 4 Gy group, whereas the 8 Gy group showed a decline, suggesting the beginning of cytotoxic effects overtaking MGCC proliferation. At 12 Gy, while multinucleated giant cells were also observed, there was a marked reduction in overall cell viability. Abnormal nuclear morphologies, such as nuclear distortion and fragmentation, were prominently seen in cells irradiated with 8 Gy and 12 Gy by day 5.

Lower doses (4 Gy) tend to induce mainly mononuclear giant cells with higher survival rates, while intermediate (8 Gy) and higher doses (12 Gy) more effectively induce MGCCs, particularly multinucleated types. However, excessive radiation (12 Gy) severely compromises cell viability, limiting its utility for extended studies.

Ionizing radiation induces giant cancer cell formation in a dose-dependent manner in HeLa cells. While 4 Gy favours mononuclear giant cells, doses of 8 Gy and 12 Gy effectively induce both mono- and multinucleated giant cells. Among these, 8 Gy offers an optimal balance between MGCC induction and cell viability, making it suitable for further mechanistic studies. Understanding MGCC behaviour may provide valuable insights into radiation resistance and cancer recurrence.

Conclusively, our study demonstrates that ionizing radiation induces the formation of mono- and multinucleated giant cancer cells in HeLa cells in a dose-dependent manner. While lower doses promote primarily mononuclear forms, higher doses, particularly 8 Gy, effectively induce therapy-resistant MGCCs without severely compromising viability. These findings underscore the importance of MGCCs in radiation response and highlight their potential role in cancer recurrence and resistance.

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