frontiers | Frontiers in Molecular Biosciences

TYPE Review
PUBLISHED 09 July 2024
DOI 10.3389/fmolb.2024.1409300

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OPEN ACCESS

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RECEIVED 29 March 2024
ACCEPTED 12 June 2024
PUBLISHED 09 July 2024

CITATION
Dagar G, Gupta A, Shankar A, Chauhan R, Macha MA, Bhat AA, Das D, Goyal R, Bhoriwal S, Pandita RK, Prasad CP, Sarkar PS, Pandita TK and Singh M (2024), The future of cancer treatment: combining radiotherapy with immunotherapy. *Front. Mol. Biosci.* 11:1409300. doi: 10.3389/fmolb.2024.1409300

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The future of cancer treatment: combining radiotherapy with immunotherapy

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Radiotherapy (RT) and immunotherapy (IT) are the powerful tools for cancer treatment which act through the stimulation of immune response, and evidence suggest that combinatorial actions of these therapies may augment each other's beneficial effect through complex synergistic mechanisms. These molecular strategies are designed to target rapidly dividing cancer cells by either directly or indirectly inducing DNA damage. However, when cells detect DNA damage, they activate a range of signalling pathways known as the DNA damage response (DDR) to repair. Strategies are being developed to interfere with the DDR pathways in cancer cells to ensure their damage-induced degeneration. The stability of a cell's genetic material is largely dependent on the efficacy of DNA repair and therefore, an in-depth understanding of DNA damages and repair mechanism(s) in cancer cells is important to develop a promising therapeutic strategies for ensuring the efficacy of damage-induced tumor cell death. In recent years, a wide range of small molecule drugs have been developed which are currently being employed to combat the DNA repair deficiencies associated with tumor cells. Sequential or concurrent use of these two modalities significantly enhances the anti-tumor response, however with a concurrent probability of increased incidence of symptomatic adverse effects. With advent of newer IT agents, and administration of higher doses of radiation per fraction, such effects are more difficult to predict owing to the paucity of randomized trial data. It is well established that anti cytotoxic-T-lymphocyte-associated antigen 4 (CTLA-4), anti- Programmed cell death protein 1(PD-1), anti-Programmed cell death one ligand 1 (PD-L1) can be safely administered with RT and many studies have demonstrated survival benefit with such combination for patients with metastatic malignancy. However, the biology of radioimmunotherapy (RT/IT) is still an open area where research need to be focused to determine optimum dosage specially the interaction of the RT/IT pathways to determine optimum dosing schedule. In the current article we have summarised the possible intracellular immunological events that might be