Proceedings of the 11th World Congress on New Technologies (NewTech'25)
Paris, France - August, 2025
DOI: 10.11159/icnfa25.001

Cancer Nanomedicine: Integrated Strategies and Therapeutic Potentials

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Extended Abstract

While radiotherapy (RT) remains an integral therapeutic modality for cancer treatment, further improving its efficacy remains challenging. This is, in part, due to the limitations imposed by normal tissue toxicity concerns. Despite RT being a highly localized treatment option, some of the dose is inadvertently deposited in the surrounding healthy tissue, thereby limiting the dose escalation required to improve patient prognosis. However, locally enhancing the effects of radiotherapy by introducing radiosensitizing agents to the tumor environment can provide an avenue to circumvent this issue. Nanotechnology has facilitated a unique opportunity to achieve this. High atomic number (Z) nanoparticles can act as radiosensitizers by locally increasing the dose deposition in cells, leading to enhanced cellular damage. Additionally, functionalizing these NPs with specific targeting ligands promotes preferential tumor accumulation relative to the surrounding normal tissue. Specifically, gold nanoparticles (GNPs) have demonstrated great promise in this regard, owing to their high Z, high biocompatibility, and chemical stability. To further improve the radiosensitization, integrating a radiosensitizing chemotherapeutic agent such as docetaxel (DTX) can offer synergistic effects. DTX arrests cells in the G2/M phase of the cell cycle, the most radiosensitive phase of the cell cycle, exhibiting a complementary radiosensitizing relationship with GNPs. Given that concurrent chemoradiotherapy is already a standard clinical approach, combining DTX with GNPs as a radiosensitizing strategy is both practical and translationally relevant. Our studies have demonstrated that administering both GNPs and DTX at clinically relevant concentrations prior to radiotherapy can significantly delay tumor growth in human xenograft mouse models compared to RT treatment alone. These findings suggest that the GNP-DTX combination could not only enhance RT efficacy, but it could also enable radiotherapy dose de-escalation strategies in attempts to reduce normal tissue toxicity and improve patients' quality of life.