Localized Delivery of FePt Nanoparticles to Enhance Radiosensitivity: Inducing Ferroptosis and Shaping Immune Regulation in the Tumor Microenvironment

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Abstract

Recent advancements in cancer treatment have seen significant progress in utilizing nanomedicine, particularly nanoparticles (NPs), for local delivery within the tumor microenvironment (TME) to avoid systemic toxicity. In this study, we investigated the local delivery of FePt NPs through intra-arterial (IA) administration within the tumor site and its effect on T cells infiltration. The FePt NPs were strategically administered in conjunction with radiotherapy to explore their potential in inducing ferroptotic damage-associated molecular patterns (DAMPs) release. Our findings revealed that the local delivery of FePt NPs, in combination with radiotherapy, resulted in a significant increase in T cell infiltration within the TME. Importantly, we observed that the presence of FePt NPs induced ferroptosis, leading to the release of DAMPs, such as ATP and HMGB1. The induction of ferroptosis and subsequent release of DAMPs played a crucial role in triggering an immune response within the TME. This response was characterized by enhanced T cell infiltration, suggesting a potential mechanism for improving the efficacy of cancer immunotherapy. Local delivery of FePt NPs, in combination with radiotherapy, offers a promising strategy for enhancing T cell infiltration in the tumor microenvironment. The induction of ferroptotic DAMPs release provides a novel pathway to stimulate immune responses, ultimately improving the therapeutic efficacy of cancer treatment.

Keywords

Iron-platinum nanoparticles, Tumor microenvironment, Ferroptosis, Damage-associated molecular patterns, Intra-arterial (IA) administrated model.