The combination of chemo- and immunotherapy represents one promising strategy to overcome the existent challenges in the present-day anticancer therapy. Here, spermine-modified acetalated dextran nanoparticles (Sp-AcDEX NPs), co-loaded with the non-genotoxic molecule Nutlin-3a (Nut3a), and the cytokine granulocyte-macrophage colony-stimulating factor (GM-CSF), are developed to induce cancer cell death and create a specific antitumor immune response. These polymeric NPs release Nut3a in a pH dependent fashion and induce endosomal escape. Due to Nut3a, the loaded NPs exert specific toxicity toward wild-type p53 cancer cells while avoiding toxicity in immune cells. Furthermore, the NPs show intrinsic immune adjuvancy on monocyte derived-dendritic cells, upregulating the expression of cell surface CD83 and CD86 costimulatory markers. Finally, it is examined that by inducing MCF-7 breast cancer cell death and acting as immune adjuvants, the NPs can downregulate the expression of IL-10 and upregulate IL-1β, leading to proliferation of CD3⁺ and cytotoxic CD8⁺ T cells. Overall, the study suggests that Sp-AcDEX NPs loaded with Nut3a and GM-CSF is a promising system for chemo-immunotherapy, capable of inducing tumor cell death and stimulating immune response.
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