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Immunomodulatory properties of nickel-doped ferric-based nanoparticles in vitro

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Abstract

Iron-based nanoparticles (NPs) represent small nanocarriers made of iron oxides. These nanoparticles include magnetite NPs (Fe_3O_4), maghemite NPs (γ-Fe_2O_3), or mixed ferrites (metal-doped iron oxide NPs; MFe_2O_4, where M can be Co, Ni, Zn, or Mn). Due to their unique characteristics, including biocompatibility, reported selective toxicity towards cancer cells, magnetic imaging capabilities, and hyperthermic properties, they are regarded as a promising modality for cancer treatments. In this context, it is crucial to assess the impact of these NPs on immune anti-cancer responses, as immunosuppressive effects on immune cells are undesirable in cancer therapies and may compromise the outcome of the treatment.

For this purpose, we initially investigated the direct anti-cancer effects of FN NPs (ferric oxide-based NPs doped with Ni) on the CT26 (murine colorectal adenocarcinoma) cell line. To evaluate the immune response to the treated cancer cells, syngeneic bone marrow-derived dendritic cells (BMDCs) were pulsed with the lysates of FN NP-pretreated CT26 cells. These BMDCs were maturated overnight and analyzed by flow cytometry for expression of maturation markers. A portion of the prepared BMDCs was additionally co-cultured with T cells, and their activation was assessed by examining the production of IFN-γ and TNF-α, along with the expression of PD-1 and TIM-3 using flow cytometry.

Our experiments demonstrated that FN nanoparticles exhibit a direct, dose-dependent toxic effect and an increased apoptotic rate in the CT26 cancer cell line. No immunosuppressive effects were detected concerning the expression of maturation markers of FN NP-CT26-pulsed and maturated BMDCs or their functional capacity to activate syngeneic T cells. The activation of T cells was demonstrated by the production of pro-inflammatory IFN-γ and TNF-α. Moreover, no changes were detected in the expression of PD-1 and TIM-3 checkpoint molecules linked with the exhausted T cell phenotype.

In conclusion, the evaluated FN NPs displayed direct anti-cancer toxicity within our experimental model while preserving the immune response to the cancer cells. These findings imply that the nanoconstruct may be a viable candidate for anti-cancer interventions.