Documents

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Combination of local immunogenic cell death-inducing chemotherapy and DNA vaccine increases the survival of glioblastoma-bearing mice

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Abstract
Immunotherapy efficacy as monotherapy is negligible for glioblastoma (GBM). We hypothesized that combining therapeutic vaccination using a plasmid encoding an epitope derived from GBM-associated antigen (pTOP) with local delivery of immunogenic chemotherapy using mitoxantrone-loaded PEGylated PLGA-based nanoparticles (NP-MTX) would improve the survival of GBM-bearing mice by stimulating an antitumor immune response. We first proved that MTX retained its ability to induce cytotoxicity and immunogenic cell death of GBM cells after encapsulation. Intratumoral delivery of MTX or NP-MTX increased the frequency of IFN-γ-secreting CD8 T cells. NP-MTX mixed with free MTX in combination with pTOP DNA vaccine increased the median survival of GL261-bearing mice and increased M1-like macrophages in the brain. The addition of CpG to this combination abolished the survival benefit but led to increased M1 to M2 macrophage ratio and IFN-γ-secreting CD4 T cell frequency. These results highlight the benefits of combination strategies to potentiate immunotherapy and improve GBM outcome. © 2023

Author Keywords
Combination immunotherapy; DNA vaccine; Glioblastoma; Immunogenic cell death; Mitoxantrone; PLGA nanoparticle

Index Keywords
Chemotherapy, DNA, Epitopes, Macrophages, Mammals, Nanoparticles, T-cells, Vaccines; Combination immunotherapy, DNA vaccine, Glioblastomas, Immunogenic cell death, Local delivery, Mitoxantrone, Mono-therapy, Pegylated, Plasmid encoding, PLGA nanoparticles; Cell death; adenosine triphosphate, calreticulin, DNA vaccine, gamma interferon, interleukin 10, interleukin 1beta, interleukin 6, macrogol 2000, mitoxantrone, monocyte chemotactic protein 1, polyglactin, polymer nanoparticle, tumor necrosis factor, DNA vaccine; animal cell, animal experiment, animal model, animal tissue, Article, cancer immunization, cancer model, cancer survival, CD3+ T lymphocyte, CD4+ T lymphocyte, CD8+ T lymphocyte, cell viability, cell viability assay, controlled study, cytokine release, cytotoxicity, DNA immunization, evaporation, female, fluorescence activated cell sorting, gene frequency, GL261 cell line, glioblastoma, IC50, immunogenic cell death, in vitro study, in vivo study, intratumoral drug administration, local therapy, long term survival, M1 macrophage, M2 macrophage, median survival time, mouse, nanoencapsulation, nonhuman, PEGylation, survival rate, survival time, sustained drug release, ultracentrifugation, zeta potential, animal, brain tumor, glioblastoma, immunogenic cell death, immunotherapy, metabolism, procedures, tumor cell line; Animals, Brain Neoplasms, Cell Line, Tumor, Glioblastoma, Immunogenic Cell Death, Immunotherapy, Mice, Vaccines, DNA

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