Revolutionizing Glioblastoma Immunotherapy with Advanced Adjuvant Cancer Nanovaccines

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Over the past decade, interleukin 12 (IL-12) has emerged as a promising cytokine for anti-cancer immunotherapy, owing to its ability to stimulate interferon-γ production, reduce angiogenesis, and shift the cancer microenvironment towards a more favorable composition characterized by increased TH1 cells and inflammatory M1-type macrophages, while decreasing TH0 and M2-type phenotype macrophages[1]. However, the clinical utility of IL-12 as a systemic cancer treatment is hindered by its significant toxicity, instability, and short half-life. In our laboratory, we have tackled these challenges by encoding IL-12 into self-amplifying RNA (saRNA) and delivering it via lipid nanoparticles (LNP) and polymeric nanoparticles, thereby creating adjuvant cancer nanovaccines aimed at improving glioblastoma (GBM) treatment[2]. These formulations were administered intratumorally to target tumor-associated macrophages (TAMs) and modulate the TAM landscape.

Our research has resulted in the successful formulation of this adjuvant cancer nanovaccine. *In vitro* studies have demonstrated that the nanoparticle vaccine is non-toxic to both GBM cancer cells and mouse macrophages[3]. Importantly, the presence of nanoparticles has been shown to induce the production of pro-inflammatory cytokines (such as IL-6, IL-8) in murine GBM cancer cells and macrophages (TNF-α and IL-6), suggesting a potential modulation of the TAM landscape. This effect was further corroborated by mRNA expression analysis using RT-PCR, which revealed an increase in the production of pro-inflammatory cytokines IL-8 and IL-6 with the PLGA nanoparticle vaccine. Furthermore, various doses of saRNA were tested in murine GBM cell lines and murine macrophages, resulting in higher expression of IL-12 after 72 hours of transfection. These findings highlight the promising potential of our approach in enhancing immunotherapy for GBM and underscore the importance of nanoparticle-based delivery systems in cancer treatment strategies.

References

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