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Multimodal neuro–nanotechnology: Challenging the existing paradigm in glioblastoma therapy

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Abstract

Integrating multimodal neuro- and nanotechnology-enabled precision immunotherapies with extant systemic immunotherapies may finally provide a significant breakthrough for combatting glioblastoma (GBM). The potency of this approach lies in its ability to train the immune system to efficiently identify and eradicate cancer cells, thereby creating anti-tumor immune memory while minimizing multi-mechanistic immune suppression. A critical aspect of these therapies is the controlled, spatiotemporal delivery of structurally defined nanotherapeutics into the GBM tumor microenvironment (TME). Architectures such as spherical nucleic acids or poly(beta-amino ester)/dendrimer-based nanoparticles have shown promising results in preclinical models due to their multivalency and abilities to activate antigen-presenting cells and prime antigen-specific T cells. These nanostructures also permit systematic variation to optimize their distribution, TME accumulation, cellular uptake, and overall immunostimulatory effects. Delving deeper into the relationships between nanotherapeutic structures and their performance will accelerate nano-drug development and pave the way for the rapid clinical translation of advanced nanomedicines. In addition, the efficacy of nanotechnology-based immunotherapies may be enhanced when integrated with emerging precision surgical techniques, such as laser interstitial thermal therapy, and when combined with systemic immunotherapies, particularly inhibitors of immune-mediated checkpoints and immunosuppressive adenosine signaling. In this perspective, we highlight the potential of emerging treatment modalities, combining advances in biomedical engineering and neurotechnology development with existing immunotherapies to overcome treatment resistance and transform the management of GBM. We conclude with a call to action for researchers to leverage these technologies and accelerate their translation into the clinic.

Keywords: glioblastoma; immunotherapy; neuro-nanotechnology.