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Local immunotherapy of glioblastoma: A comprehensive review of the concept

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Abstract

Despite advancements in standard treatments, the prognosis of Glioblastoma (GBM) remains poor, prompting research for novel therapies. Immunotherapy is a promising treatment option for GBM, and many immunotherapeutic agents are currently under investigation. Chimeric antigen receptor (CAR) T cells are rapidly evolving in immunotherapy of GBM with many clinical trials showing efficacy of CAR T cells exerting anti-tumor activity following recognition of tumor-associated antigens (TAAs). Exhaustion in CAR T cells can reduce their capacity for long-term persistence and anti-tumor action. Local immunotherapy, which targets the tumor microenvironment and creates a more hospitable immunological environment for CAR T cells, has the potential to reduce CAR T cell exhaustion and increase immunity. Tertiary lymphoid structures (TLS) are ectopic lymphoid-like formations that can develop within the tumor microenvironment or in other non-lymphoid tissues. As a comprehensive local immunotherapy tool, the incorporation of TLS into an implanted biodegradable scaffold has amazing immunotherapeutic potential. The immune response to GBM can be improved even further by strategically inserting a stimulator of interferon genes (STING) agonist into the scaffold. Additionally, the scaffold's addition of glioma stem cells (GSC), which immunotherapeutic approaches may use to target, enhances the removal of cancer cells from their source. Furthermore, it has been demonstrated that GSCs have an impact on TLS formation, which helps to create a favorable tumor microenvironment. Herein, we overview local delivery of a highly specific tandem AND-gate CAR T cell along with above mentioned components. A multifaceted approach that successfully engages the immune system to mount an efficient targeted immune response against GBM is provided by the integration of CAR T cells, TLS, STING agonists, and GSCs within an implantable biodegradable scaffold. This approach offers a promising therapeutic approach for patients with GBM.

Keywords: Glioblastoma; Immunotherapy; Local delivery; Management.