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CAR-engineered NK cells versus CAR T cells in treatment of glioblastoma; strength and flaws

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Abstract

Glioblastoma (GBM) is a highly aggressive primary brain tumor that carries a grim prognosis. Because of the dearth of treatment options available for treatment of GBM, Chimeric Antigen Receptor (CAR)-engineered T cell and Natural Killer (NK) therapy could provide alternative strategies to address the challenges in GBM treatment. In these approaches, CAR T and NK cells are engineered for cancer-specific immunotherapy by recognizing surface antigens independently of major histocompatibility complex (MHC) molecules. However, the efficacy of CAR T cells is hindered by GBM's downregulation of its targeted antigens. CAR NK cells face similar challenges, but, in contrast, they offer advantages as off-the-shelf allogeneic products, devoid of graft-versus-host disease (GVHD) risk as well as anti-cancer activity beyond CAR specificity, potentially reducing the risk of relapse or resistance. Despite CAR T cell therapies being extensively studied in clinical settings, the use of CAR-modified NK cells in GBM treatment remains largely in the preclinical stage. This review aims to discuss recent advancements in NK cell and CAR T cell therapies for GBM, including methods for introducing CARs into both NK cells and T cells, addressing manufacturing challenges, and providing evidence supporting the efficacy of these approaches from preclinical and early-phase clinical studies. The comprehensive evaluation of CAR-engineered NK cells and CAR T cells seeks to identify the optimal therapeutic approach for GBM, contributing to the development of effective immunotherapies for this devastating disease.

Keywords: Antigen specificity; CAR T cells; Glioblastoma; Immunotherapy; NK cells; Preclinical studies.