Novel mechanisms and approaches in immunotherapy for brain tumors.

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Abstract

Converging data indicate that the immune system is able to recognize cancer epitopes as non-self and mount an immune reaction that may erase, or temporarily block, tumor growth. The immune pressure supports the amplification of immune resistant tumor clones, creating an immune suppressive environment that leads to the formation of a clinically relevant tumor. These general observations also apply to brain tumors and specifically to gliomas. Cancer immunotherapy strategies are aimed at reverting such immune suppression. Two approaches are already used in the clinics. The first one, peptide immunotherapy, has been oriented to the most aggressive glioma, glioblastoma (GBM) where, in the context of EGFR (epidermal growth factor receptor) amplification, a large deletion arises and creates a novel, cancer-specific antigen, EGFRvIII. The second one is dendritic cell immunotherapy. Dendritic cells are potent antigen presenting cells that can be pulsed with autologous tumor lysate or peptide pp65 from cytomegalovirus (CMV) that is present in GBM but not in normal brain. Antigen presentation by dendritic cells is bolstered by preconditioning their injection site with the tetanus/diphtheria toxoid. The third approach is adoptive cell therapy (ACT) in which tumor-specific T cells can be amplified ex vivo and subsequently re-injected to the patient to lyse cells expressing tumor antigens, increasing survival durably in a fraction of melanoma patients. ACT may also be based on T cell transduction of tumor specific receptors or chimeric antigen receptors (CARs). CARs are powerful tools for immunotherapy but off-target toxicity may be an issue as they do not request MHC presentation for activation. Upcoming clinical trial results will clarify the most effective direction for cancer immunotherapy in gliomas and other cancers with poor prognosis.


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