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Investigating TCR T Cell Migration and Cytotoxicity Using 3D Bioprinting

Genetic engineering of T cells to express tumor antigen-specific T cell receptors (TCRs) is a promising approach in cancer immunotherapy. While the cytotoxic potential against cancer of these engineered TCR T cells is critical, their therapeutic efficacy also depends on their ability to migrate, infiltrate, proliferate, and persist within the complex tumor microenvironment (TME). This is particularly challenging in solid tumors, where the TME comprises a heterogeneous mix of stromal cells, immune-suppressive factors, and extracellular matrix components that hinder T cell function. To address these challenges, we evaluate the multifaceted functionality of TCR T cells using 3D bioprinted fully human models. Using a single-chain TCR (scTCR) specific for the HLA-A2.1-restricted p53(264-272) epitope as a model, we encapsulated TCR T cells and p53-high tumor cells in the hydrogel to assess anti-tumor efficacy of the TCR T cells.
This 3D bioprinted tissue allows both end-point histological evaluation and real-time live-cell imaging, providing a versatile platform for studying immune-tumor interactions. Immunohistochemical (IHC) analysis of the formalin-fixed paraffin-embedded (FFPE) tissue revealed that TCR T cells effectively eradicated about 40 % of tumor cells in both the single-cell model and the tumor-spheroid model within two days. Furthermore, analysis of the tumor spheroid model showed that CD8+ T cells constituted the majority of tumor-infiltrating immune cells. Interestingly, multiplex cytokine profiling revealed a robust induction of Th1 cytokines (e.g., IFN-γ, TNF-α) and chemokines (e.g., CXCL9, CXCL10, RANTES).
This 3D bioprinted model represents a significant advancement in preclinical modeling, enabling the evaluation of TCR T cell migration, infiltration, and cytotoxicity within a physiologically relevant TME. By incorporating additional immune components, this model holds promise for optimizing engineered T cell therapies and identifying strategies to overcome TME-mediated suppression, ultimately accelerating the development of effective cellular immunotherapies for solid tumors.

Research type

Translational research

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