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Identifying cancer-specific T cells for TCR T-cell immunotherapy through engineered proteins

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The identification of cancer-specific T cell receptor (TCR) sequences is crucial for advancing cancer immunotherapies. Recent studies and clinical trials have revealed a vulnerability in monoclonal T cell therapy, where cancer cells can evade the immune response through the loss of HLA heterozygosity and low antigen heterogeneity. To address this challenge, cocktail T cell therapy using TCRs that target multiple HLAs and antigens has been proposed to enhance the efficacy of adoptive T cell transfer therapy. In pursuit of this goal, we have developed peptide-bound major histocompatibility complex (pMHC) proteins in the form of single-chain-trimers (SCTs). This innovative platform allows for the rapid and high-throughput identification and isolation of cancer-targeting CD4+ and CD8+ T cells targeting a wide array of HLAs and cancer antigens. The identified antigen-specific TCRs are subsequently sequenced, validated for functionality, and assessed for potential therapeutic applications. We applied this technology to PBMCs extracted from patients with HPV-16-related precancerous conditions in a clinical trial. We successfully identified cancer-specific TCRs, which are currently undergoing pre-clinical validations for their safety and efficacy in CRISPR-mediated TCR T cell therapy. In summary, the application of the SCT technology holds significant value for fundamental immune-oncology studies and contributes to the advancement of immunotherapy for cancer.

SESSION: Novel Strategies in CAR T Therapies (PM)