ENGINEERED CAR T CELL THERAPY FOR SOLID TUMORS

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The adoptive transfer of T cells redirected to tumor-associated antigens via transgenic expression of chimeric antigen receptors (CARs) has produced impressive clinical responses in patients with hematologic malignances. However the successful extension of this therapy to solid tumors has proven challenging due to i) the paucity of target antigens that are tumor selective, leading to a heightened risk of "on-target, off-tumor" toxicities and, ii) the suppressive tumor microenvironment, which subverts T cell effector function. Therefore, to overcome these limitations we have programmed T cells with a combination of receptors that recognize a gene expression pattern that is unique to the tumor site and whose endodomains deliver intracellular signals 1, 2 and 3 (antigen, co-stimulation and cytokine) required for optimal T cell activation and protection from suppressive factors present at the tumor site. The current presentation will not only highlight our T cell engineering improvements but also our process optimization, including the incorporation of the G-Rex device, to facilitate the clinical and commercial development of potentially curative therapies.