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Application of chimeric antigen receptors approach as a tool to treat infectious diseases and chronic pain

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CD6 (NTR) has extracellular SRCR domains that play an important role in recognizing the antigen T cells proliferation and expansion. However, SNP induced glycosylation of SRCR domains perturbed T cells proliferation, so CAR modified CD6 receptor will be an ideal choice having immunoglobulin ScFvs chain as ectodomain along with integration of different C-terminal subunits (CD3-ζ, CD28 and 4-1BB). CARs offer a wider range of functional properties than conventional T cell receptors (TCR). Whilst the transduction may exploit a variety of methods, stable gene transfer is essential for persistent CAR expression in T cells. For engineering of CARs, we will transduce 2B4 hybridoma cells by using retroviral transduction technique with same CD6-specific CAR encoding different CD3-ζ, CD28 and 4-1BB endodomains from different T cell products. Effector protein such as SLP-76 having SH2 domain binding site for phosphorylated tyrosine is also involved in mounting immune response. To evaluate the interaction between SLP-76 peptide and CAR-T cells (CD6) having CD3-ζ, CD28 and 4-1BB cytoplasmic domains, approach (Coprecipitation Analysis and confirmation by western blotting) will be used. Surface plasmon resonance method will be employed to measures the interaction between ligand/antigen specific tumor cells and antigen binding domain (ScFv) of newly CAR modified CD6-T cells to see whether it induces efficient and persistence T-cells proliferation: And autocrine functional productions of interleukins (IL-2 measure by cellular assays). Our aims and objective is also to study: How costimulation affects T-cell fate in CD6 dependent CAR-mediated activity in T-cell? we will infuse two or more T-cells products with identical CARs specificity by developing specific CAR costimulatory moiety having different costimulatory components using different T-cells subsets. Ultimately, we will evaluate costimulatory activity in vivo expansion of different CD6-specific CAR-T cells. To summarize, CAR based modulation of NTRs has a broader implication in clinical perspective for potential immune based therapeutics.

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