Gene Editing of CAR-T Cells for the Treatment of T Cell Malignancies

Background: T-cell malignancies include T-cell acute lymphoblastic leukemia (T-ALL) and T-cell non-Hodgkin’s lymphoma (T-NHL). Despite improved treatments over the past two decades there is still a high rate of relapse. Recently, genetically modified T-cells expressing chimeric antigen receptors (CAR-T) have been used to target antigens on B-cell malignancies. The benefit of these approaches has been dramatic and long-term remissions in relapsed B-cell malignancies have been observed. Until now, targeting of T-cell malignancies using CAR-T has not been explored due to challenges with shared antigens between normal T-cells used to carry CARs and the T-cell malignancies themselves. This results in “fratricide” of the CAR-Ts.

Technology Description: We have developed a series of CAR-Ts (figure below) expressing high affinity CAR to CD7 as well as other T cell antigens (CD2, CD5, CD4). Our technology also incorporates a suicide gene (CD34-TK75) to allow for tracking of these genetically modified T-cells. In addition, the ability to delete the T-cell receptor alpha allows for the use of non-self T-cells (allogeneic) for treatment without concern for alloreactivity or graft-versus-host disease. We believe that our technology may allow for the treatment of T cell hematologic malignancies with comparable clinical efficacy to that see for CD19 CAR-T treatment currently available for B-cell malignancies.

Applications: Treatment of T-cell malignancies

Field: Oncology

Stage of Development: We have demonstrated that our CAR-Ts result in high efficiency (>90%) of CD7 deletion and ~80% biallelic deletion of both CD7 and T cell receptor alpha in vitro. Our mice data suggest that our CD7 CAR-T are effective at eliminating multiple CD7+ T-ALL cell lines and multiple primary T-ALL patient xenografts in vivo without any signs of xenogeneic graft vs host disease. We are currently generating clinical grade virus for the first-in-man studies to test this therapeutic reagent in man.

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