INTRODUCTION

CAR T cell products are in early clinical development for the treatment of hematological malignancies and solid tumors. CARs can induce superior antitumor activity when compared to existing therapies. However, the translation of CAR T cells to the clinic has been limited by a number of challenges, including the difficulty of generating large numbers of T cells, their inability to differentiate into memory cells, and the limited duration of antitumor activity. This has led to the development of next-generation CAR T cell products that are designed to address these limitations. In this manuscript, we report the development of a novel CAR T cell product that is designed to overcome these challenges and is capable of effective antitumor activity in vivo. We demonstrate that this product is capable of inducing significant antitumor activity in a variety of in vivo models, including a xenograft model of human cancer.

METHODS

We employed SDT CAR to enrich live T cells and utilized GEMO CAR to enrich for CAR-expressing T cells. We then performed a comprehensive analysis of the CAR T cell product, including efficacy studies in vitro and in vivo, and compared it to existing CAR T cell products.

CD70-containing CAR design (CD70 CAR)

CD70 CAR was designed to enable CAR T cell product to express and target the CD70 molecule. CD70 is a transmembrane ligand that is expressed on the surface of many cell types, including tumor cells. We used the CD70 molecule as a target for our CAR T cell product because it is not expressed on healthy cells, and because it is expressed on a wide variety of tumor cells. We then evaluated the efficacy of CD70 CAR in vitro and in vivo, and compared it to existing CAR T cell products.

Generation of allogeneic CD70 CAR V51 T cells

We generated CD70 CAR V51 T cells using SDT CAR and GEMO CAR. SDT CAR was used to express the CD70 molecule, and GEMO CAR was used to express the CAR T cell product. We then evaluated the efficacy of CD70 CAR V51 T cells in vitro and in vivo, and compared it to existing CAR T cell products.

T cell memory, NK, chemokine, receptor, and activation/exhaustion expression profile in CD70 CAR V51 T cells

We evaluated the expression of T cell memory, NK, chemokine, receptor, and activation/exhaustion markers in CD70 CAR V51 T cells. We found that CD70 CAR V51 T cells were enriched for T cell memory and NK activation markers, and were depleted for T cell exhaustion markers.

CD70 CAR V51 T cells express potent cytotoxic activity against various CD70+ solid tumor cell lines

We evaluated the cytotoxic activity of CD70 CAR V51 T cells against a variety of CD70+ solid tumor cell lines. We found that CD70 CAR V51 T cells were able to effectively kill CD70+ tumor cells, and were more cytotoxic than existing CAR T cell products.

Summary and conclusions

CD70 CAR V51 T cells are a novel CAR T cell product that is designed to overcome the limitations of existing CAR T cell products. We demonstrate that CD70 CAR V51 T cells are able to effectively kill CD70+ tumor cells, and are more cytotoxic than existing CAR T cell products. We also demonstrate that CD70 CAR V51 T cells are able to improve antitumor activity in vivo, and are a promising new CAR T cell product for the treatment of solid tumors.