A chimeric antigen receptor (CAR) that works by using an anti-CD83 scFv region to enable a T cell to target CD83+ alloreactive T cells that mediate GVHD after allogeneic hematopoietic cell transplantation (alloHCT). Moreover, the CD83 CAR-T cell provides direct graft-versus-leukemia against CD83 expressing myeloid leukemia without impairs normal hematopoiesis. Essentially, this single novel cell can effectively separate GVHD from GVL without the need for nonselective pharmacologic immunosuppression.

COMMERICAL OPPORTUNITY

- Graft-versus-host-disease (GVHD) is a major cause of non-relapse mortality in patients receiving alloHCT, of which approximately 8,000 are performed in the US annually. GVHD is caused by alloreactive donor T cells. GVHD prevention typically includes immunosuppressive drugs that broadly suppress donor T cells. However this approach also impairs beneficial regulatory T cells (Treg) required for immune tolerance and cytotoxic T lymphocytes (CTL) that mediated the anti-tumor activity of the transplant.

- Ultimately, GVHD can add a cost of up to $67,000 to the treatment of a patient who has undergone a transplant. Around 40-60% of HSCT recipients will develop aGVHD. 20% of GVHD cases result in death. The number of patients likely to develop GVHD within 100 days of the transplant in the United States alone can be as great as 4,000/year, bringing the market size to $268 million.

- The ability of the CD83 CAR T cell to selectively kill myeloid leukemia without impairing normal hematopoiesis further extends its clinical impact. Thus, the CD83 CAR T cell carries high likelihood to reduce transplant-related mortality and improve outcomes after alloHCT.

TECHNOLOGY

NSG mice received 25x10⁶ human peripheral blood mononuclear cells; then inoculated with CD83 CAR or mock transduced T cells (1-10x10⁶). (A) Survival is shown. Recipient mice were humanely euthanized at day +21 and tissue GVHD severity was evaluated. GVHD path scores, amount of Ki-67+, CD3+ T cells/HPF, and representative IHC images (CD3=red, Ki-67=brown) are shown for recipient (C-D) liver. **P=.001-.01. While this technology is initially being developed for GVHD it is also being adapted to treat autoimmunity, prevent allograft rejection, and facilitate lasting persistence of cell products after adoptive transfer.

PUBLICATION/PATENT

- Provisional patent application filed February 23, 2018 for Dr. Davila and Dr. Betts.