A chimeric antigen receptor-expressing T regulatory cell that interacts with CD83 expressing alloreactive T cells in order to suppress allo-sensitization. The CAR construct works by using a novel anti-CD83 scFv region and intracellular signaling regions to enable CAR-Treg cell activation. CD83 CAR-Treg cells would target alloreactive T cells in a patient receiving a transplant. CD83 is expressed on the surface of alloreactive conventional T cells, which are implicated in GVHD pathogenesis. CD83 CAR Treg cells might overcome the barriers of HLA disparity in hematopoietic cell and solid organ donor selection, and suppress alloreactive T cells without the need for broadly suppressive calcineurin-inhibitors or glucocorticoids. This process may also allow for off the shelf CAR-T therapies to achieve lasting engraftment, avoid rejection in the setting of HLA-mismatch.

COMMERCIAL OPPORTUNITY

- For allogeneic hematopoietic cell transplantation, donor or third-party Tregs can be modified with an anti-CD83 CAR construct in order to suppress alloreactive donor T cells that would cause GVHD. For a solid organ transplant, host or third-party Tregs can be modified with an anti-CD83 CAR construct in order to suppress alloreactive T cells from the host that would reject the organ.

- Graft-versus-host-disease (GVHD) is a major cause of non-relapse mortality in patients receiving an allogenic hematopoietic cell transplantation (alloHCT), of which approximately 8,000 are performed in the US, and about 35,000 worldwide annually. Around 40-60% of HSCT recipients will develop aGVHD, and up to 20% of GVHD cases result in death. GVHD prevention typically includes immunosuppressive drugs that broadly effect 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. 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.

TECHNOLOGY

Off-the-shelf CD83 CAR Tregs offer significantly enhanced suppression of alloreactive T cells. Human, regulatory T cells (Treg) expressing a CD83 CAR or mock transduced Tregs were cultured with allogeneic mixed leukocyte reactions (T cell to DC ratio 30:1). The Tregs, T cells, and dendritic cells were entirely HLA-mismatched from each other. Alloreactive T cell proliferation was significantly reduced by CD83 CAR-Treg at all Treg:T cell dilutions, compared to mock Treg. *P<0.05, **P=0.01-0.001.

PUBLICATION/PATENT

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

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LICENSING OPPORTUNITY

19MB042.2019.07