HLA disparate (off the shelf) anti-CD83 CAR-T cells can kill alloreactive T cells without being rejected themselves. Moreover, it is likely that the anti-CD83 CAR-T cells could protect a second allogeneic CAR-T cell from rejection, essentially allowing any allogenic CAR-T cell, or cell therapy in general, to be used “off the shelf.” Further, CD83 CAR-T cell technology could be translated to prevent or treat solid organ allograft rejection or graft-versus-host disease as an off-the-shelf therapy. Thus, CD83 CAR-T cells could improve survival for cancer and transplant patients alike.

COMMERCIAL OPPORTUNITY

- CAR T cells have demonstrated remarkable activity for treating relapsed/refractory acute lymphoblastic leukemia and diffuse large B cell lymphoma; profoundly changing the landscape for treating aggressive hematologic malignancies. However, CAR T cell therapy is limited by the time needed to generate these cells; often relying upon host T cells acquired from heavily pre-treated patients. We designed an innovative strategy to universally permit the use of banked, off the shelf CAR T cells to rapidly treat patients with high quality allogeneic, engineered T cell products. Our novel CD83 CAR T cell suppresses alloreactive host T cells to prevent their rejection. Further evidence from our xenogeneic graft-versus-host disease models prove that CD83 CAR T cells can even halt xenoreactive human T cells in vivo. We propose that CD83 CAR T cells can be used as a banked cell product to protect third party CAR T cells, targeting your cancer antigen of choice, from destruction by host immunity. Thus, making banked, off the shelf CAR T cell therapy a viable and lifesaving possibility.

- The marketplace is attractive for CAR-T cell development, as Novartis received approval in August 2017 for Kymriah, its anti-CD19 CAR-T therapy for pediatric B-cell ALL. The trial had an overall response rate of 82.5% (52/63). Although the list price for Kymriah is $475,000 for a one-time treatment, Novartis has said only those patients who respond by the end of the first month will need to pay. In October 2017, Gilead’s Yescarta, an anti-CD19 CAR-T, was approved for large B-cell lymphoma and is listed at $375,000. In 2017, Gilead acquired Kite Pharma for $11.7B, and in 2018, Celgene acquired Juno Therapeutics for $9B. Juno was also developing a CD-19 CAR-T therapy.

TECHNOLOGY

Third-party, human CD83 CAR T cells suppress alloreactive T cells and are not rejected. Human DC-allostimulated T cells were cultured with third-party CD83 or CD19 CAR T cells (eGFP+) at a ratio of 10:1 for 5 days. CD83 CAR T cells expanded (Ki-67 59.1%), were not rejected, and suppressed opposing alloreactive T cells (Ki-67 5.55%, similar to unstimulated T cell controls). Conversely, CD19 CAR T cell proliferation was impaired by alloreactive T cells via rejection (Ki-67 36.8%) and did not inhibit the expansion of the alloreactive T cells.

PUBLICATION/PATENT

- PCT patent application filed February 22, 2019 for Dr. Davila and Dr. Betts.

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LICENSING OPPORTUNITY