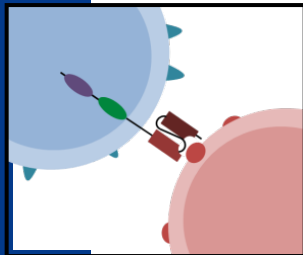


CAR-Ts with enhanced CD-28 co-stimulatory domains



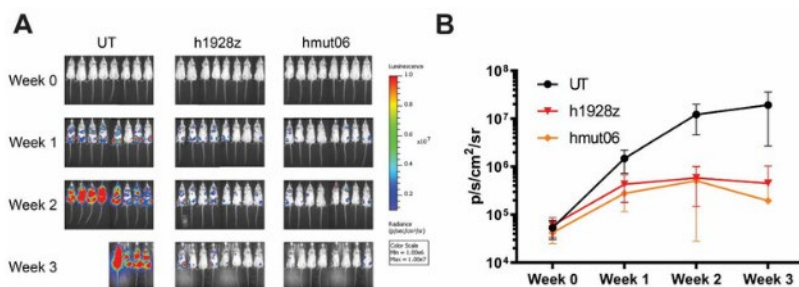
Moffitt investigators developed a chimeric antigen receptor (CAR) with enhanced CD28 costimulatory regions. The typical CD28 domain increases T-cell activation, but this often leads to exhaustion and shortened persistence. The mutated CD28 domains have mutations that optimize CAR-T-cell function while preventing exhaustion and increasing persistence. The costimulatory regions have been tested in vivo in CD19 CAR-T constructs in mouse models with the findings that mice given CAR-T cells with only a mutated CD28 endodomain had a significant survival advantage, with 100% of mice alive after 62 days compared with 50% for mice with an unmutated endodomain. Ex vivo, the mutant CAR-T cells were found to be more sensitive to antigens, possess less exhaustion related transcription factors, and enhance PD-L1 stimulation.

COMMERCIAL OPPORTUNITY

Approved CAR-T	Company	Target/Indication	2022 Drug Sales (worldwide)	Drug Price
Kymriah	Novartis	Anti-CD19 CAR-T therapy for pediatric and young adults' acute lymphoblastic leukemia (ALL), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL)	\$536M	\$475,000
Yescarta	Gilead	Anti-cd19 Car-T treatment of adult patients with large B-cell lymphoma, high-grade B-cell lymphoma, DLBCL, or FL.	\$1,160M	\$373,000
Tecartus	Gilead	Anti-CD19 CAR-T therapy for mantle cell lymphoma ("MCL") and relapsed/refractory B-cell precursor acute lymphoblastic leukemia.	\$299M	\$373,000
Breyanzi	BMS/Juno Therapeutics	Anti-CD19 CAR-T treatment for adult patients with relapsed/refractory large B-cell lymphoma.	\$182M	\$410,300
Abecma	BMS/Bluebird Bio	Anti-BCMA CAR-T therapy for multiple myeloma after four or more prior lines of therapy.	\$388M	\$481,499
Carvykti	Legend Biotech/Janssen	Anti-BCMA CAR-T therapy for patients with relapsed/ refractory Multiple Myeloma.	N/A	\$465,000

TECHNOLOGY

Antihuman CD19 mut06 CAR-T cell in vivo function. (A) hmut06 CAR-T cells have enhanced in vivo killing compared to h1928z. NSG mice were i.v. injected with 5×10^5 Raji-GFP/luc cells at week -1 and 2×10^6 CAR-T cells were i.v. injected at week 0. Mice were then measured for BLI weekly. (B) The average BLI for each week is shown for UT, hmut06, and h1928z. N=8 mice per group and representative of 2 independent experiments.



PUBLICATION/PATENT

- Provisional Patent filed for Dr. Davila

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LICENSING OPPORTUNITY



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