POSTER #4809

Development of a Novel Humanized BCMA-Directed CAR for Multiple Myeloma: Robust Activity and Low Toxicity in Preclinical Studies

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CONCLUSIONS

- **h2BCMA-BBζ T cells demonstrate strong anti-tumor activity *in vivo*, with a favorable safety profile.**
- **The optimized attributes make h2BCMA-BBζ a promising candidate for further clinical investigations.**

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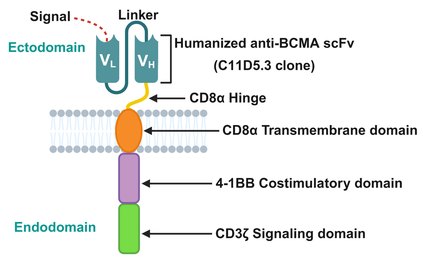
BACKGROUND AND OBJECTIVES

- CAR-T cells targeting BCMA (B-cell maturation antigen) have shown significant promise in treating relapsed/refractory multiple myeloma (r/r MM).
- Dose-limiting toxicities and safety concerns are common in heavily pre-treated patients, underscoring the need for further improvements in CAR-T therapy.
- Limited access and high costs remain major barriers to broader patient access and benefit.
- We designed and evaluated four humanized anti-BCMA CAR constructs, identifying a superior candidate with an optimal balance of safety and efficacy.

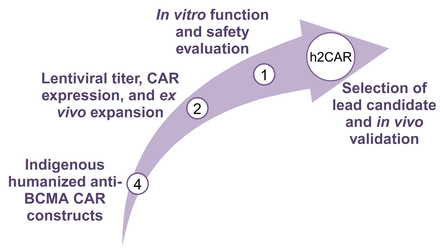
METHODS & RESULTS

Design and Selection of Novel Humanized anti-BCMA CAR

Schematic of Humanized anti-BCMA CAR

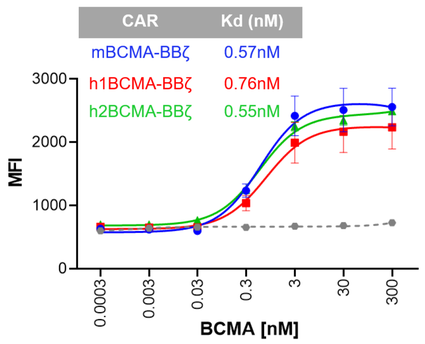


Selection pathway for lead candidate

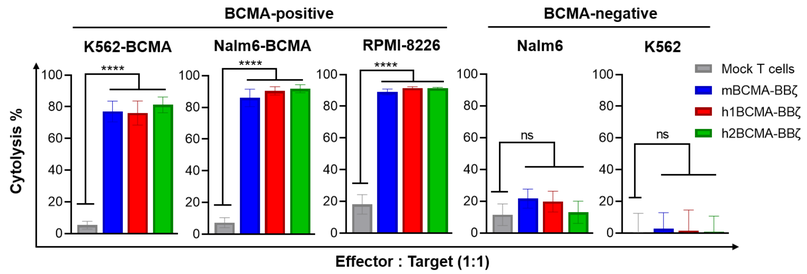


Humanized CAR-T cells maintain a binding affinity comparable to murine CAR-T

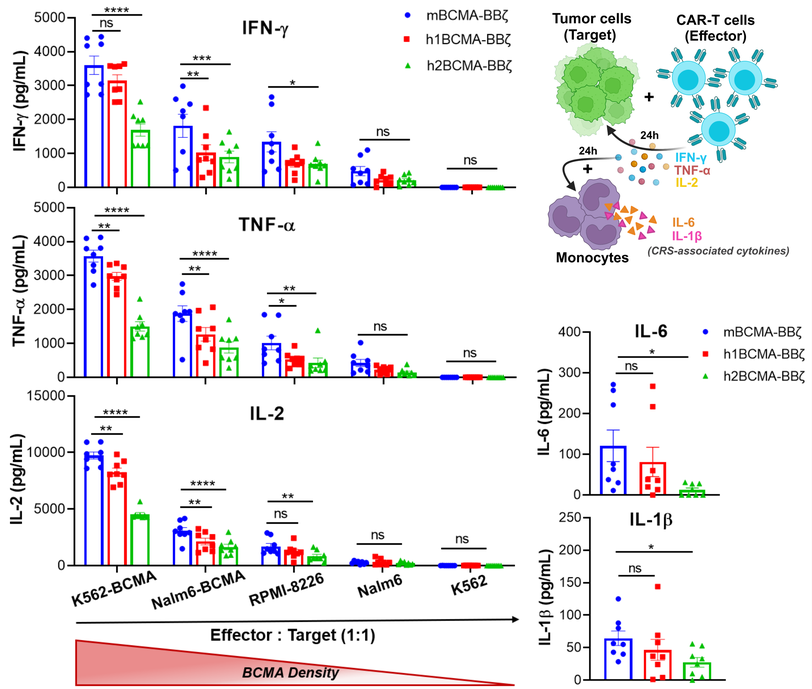
CAR	Kd (nM)
mBCMA-BBζ	0.57nM
h1BCMA-BBζ	0.76nM
h2BCMA-BBζ	0.55nM



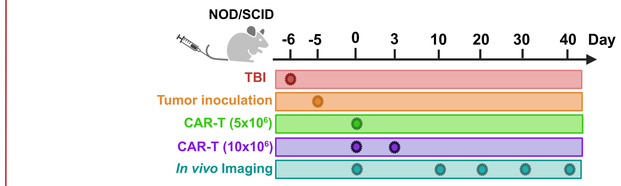
Humanized CAR-T cells selectively eliminated BCMA+ tumor cells, demonstrating efficacy comparable to murine CAR-T cells

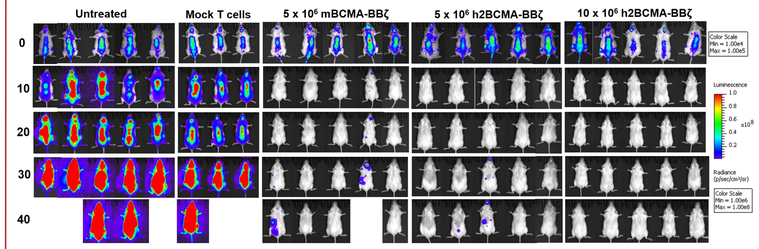


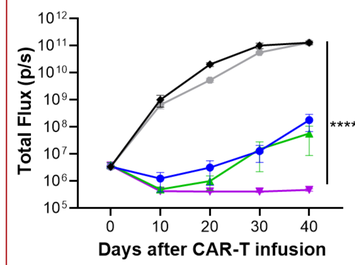
h2BCMA-BBζ T cells secreted significantly lower levels of CRS-associated cytokines

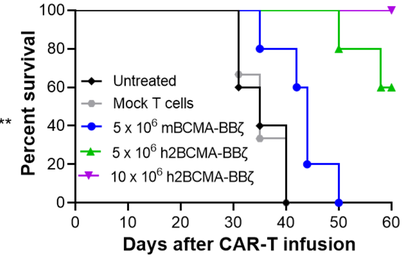


h2BCMA-BBζ T cells demonstrated potent anti-tumor efficacy and prolonged animal survival *in vivo*









- Mice treated with h2BCMA-BBζ T cells demonstrated prolonged survival, with some surviving up to 205 days.
- Mice in the mBCMA-BBζ T cell group relapsed and succumbed to disease by day 50.
- No systemic or organ-related toxicities were observed following treatment with h2BCMA-BBζ T cells.

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