Abstract #715

Anti-c-kit CAR-T Cells Afford Effective Eradication of Human AML and Normal Hematopoietic Cells in a Preclinical Model of Safer, Non-Genotoxic Stem Cell Transplant Conditioning

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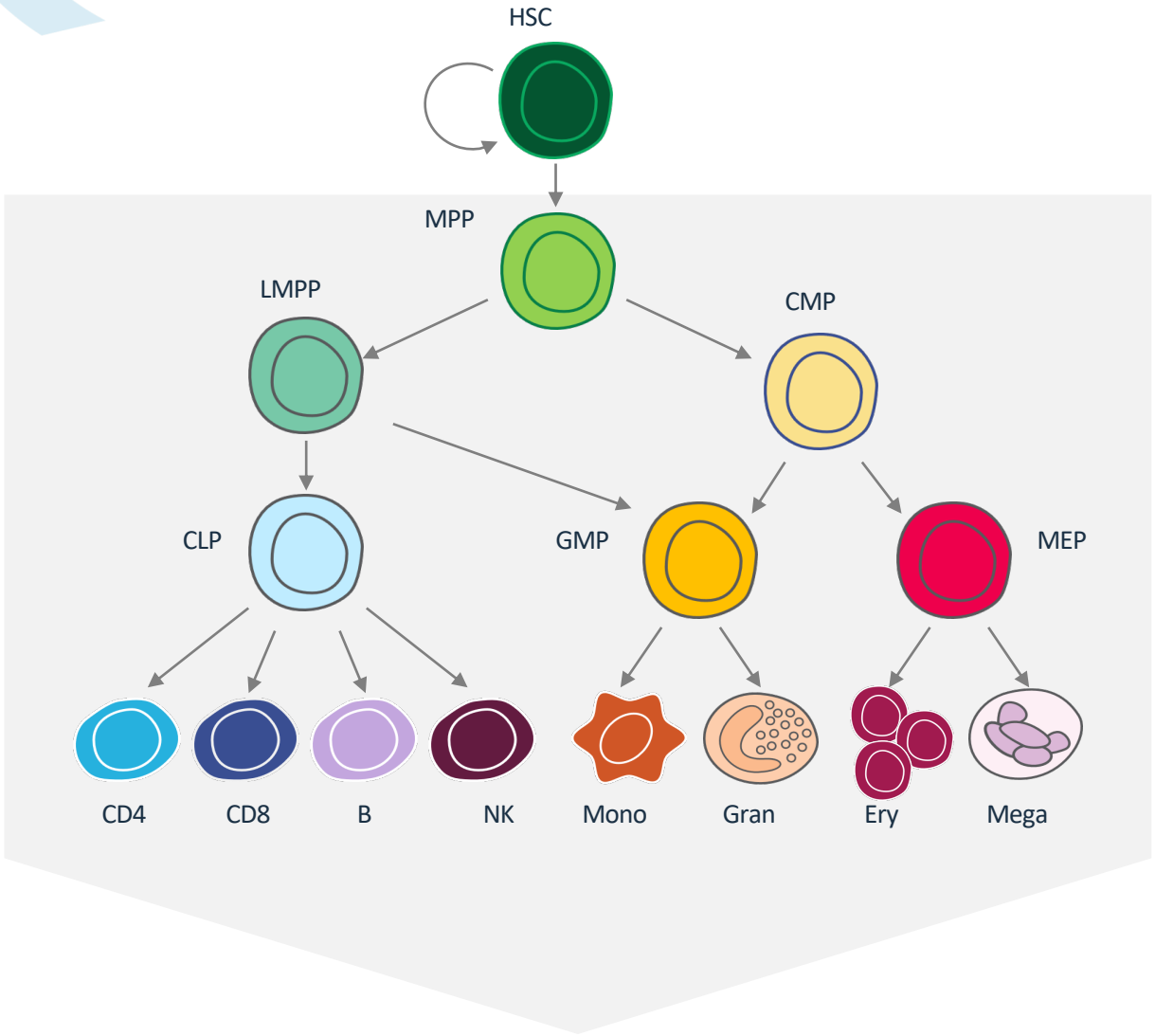
Hematopoietic Stem Cell (HSC) Transplants: The Potential to Cure



Hematopoietic stem cell transplant (HSCT) renews and re-primes the entire immune system

Risks associated with the procedure generally preclude its use except in cases of fatal disease or high unmet medical need (e.g., oncology)

A safer, more specific conditioning regimen could improve patient outcomes and greatly expand the number of indications (e.g., treatment of autoimmune diseases)

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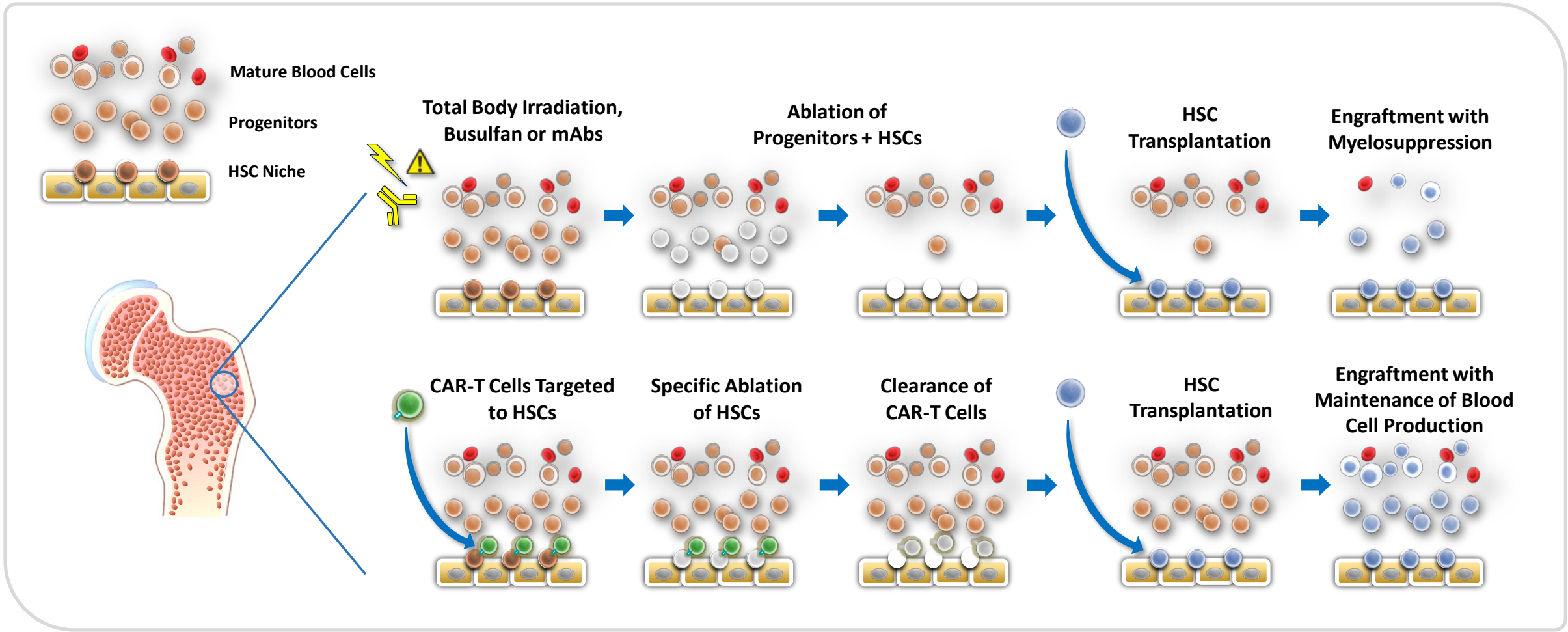
CAR-T Cells Can Effect Selective Depletion of HSCs Prior to HSCT



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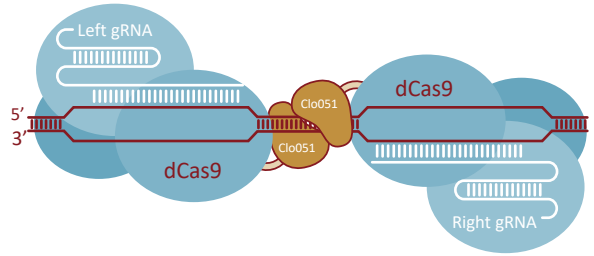
Anti-c-kit CAR-T Cells: Extending Poseida's Nonviral Allogeneic CAR-T Platform Beyond Oncology

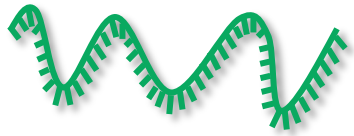
piggyBac DNA Transposon

piggyBac RNA Transposase

Cas-CLOVER gene editing system



Booster Molecule



Unique Platform Characteristics Ideally Suited to Next-Generation Applications

- Large cargo capacity enables incorporation of multiple genes including a safety switch, for efficient T cell clearance prior to transplant, and additional CAR targets
- Multiplexed gene editing and our patented booster molecule result in a fully allogeneic product with up to 100s of doses from a single production
- PiggyBac® CAR-T cells home and selectively expand in the bone marrow at the site of target stem cells
- Targeting c-kit allows broad coverage of both normal and cancerous stem cells

To learn more about our allogeneic CAR-T platform and P-BCMA-ALLO1 please visit poster #789

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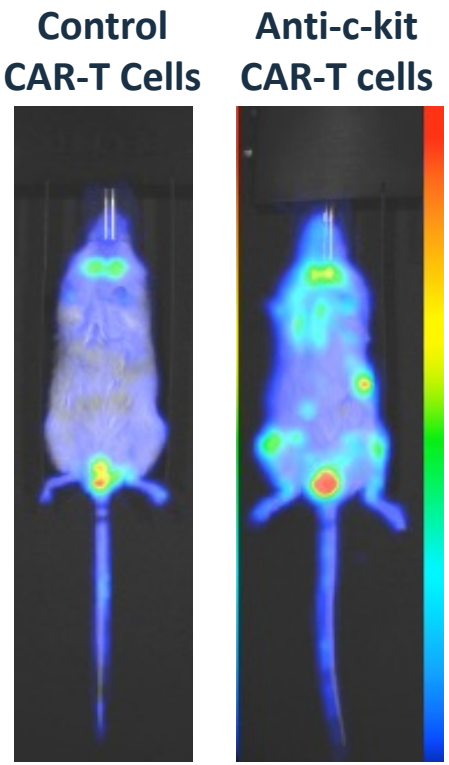
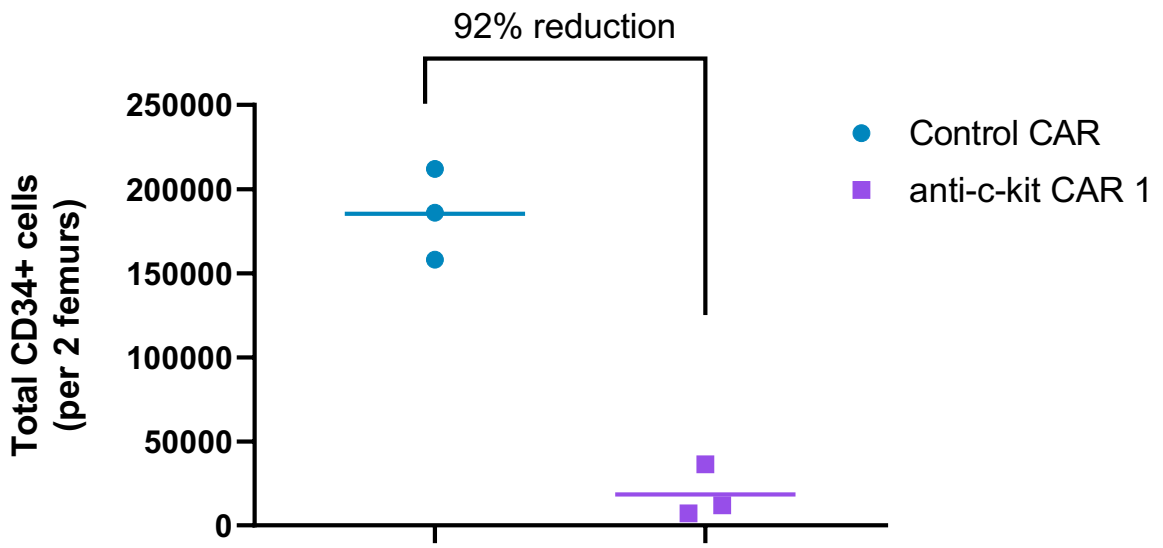
Anti-c-kit CAR-T Cells Accumulate in Bone Marrow of Humanized Mice and Deplete human HSPCs





Luciferase labelled CAR-T cells traffic to the bone marrow of humanized mice where they proliferate and kill human CD34+ stem and progenitor cells with >90% depletion measured 48 hours post-transplant

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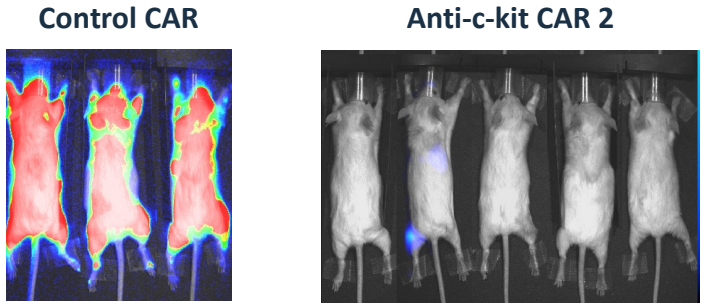
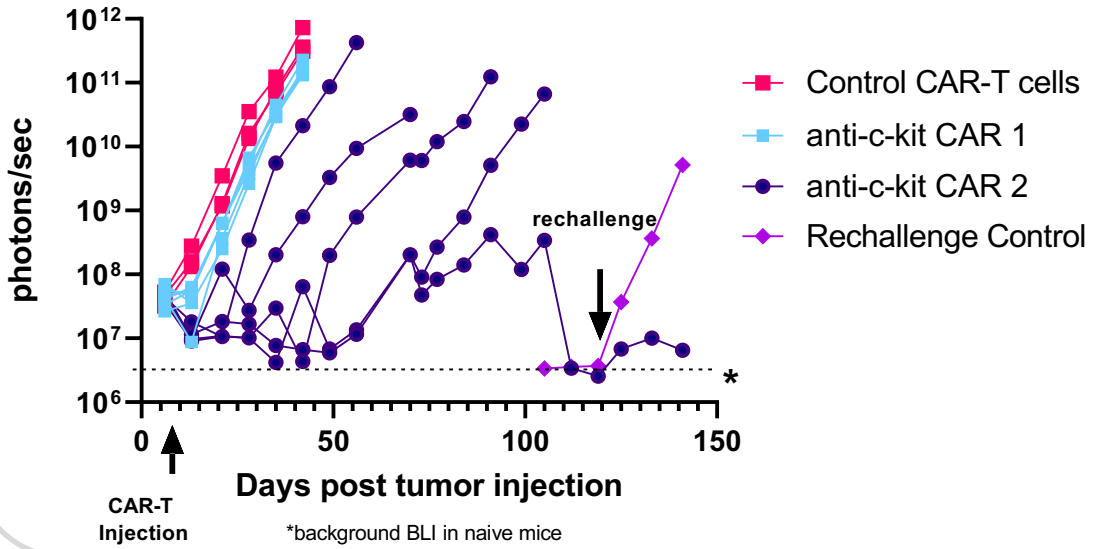
Anti-c-kit CAR-T Cells Effect Prolonged AML Tumor Control

Whole body flux at 28 days post-tumor injection

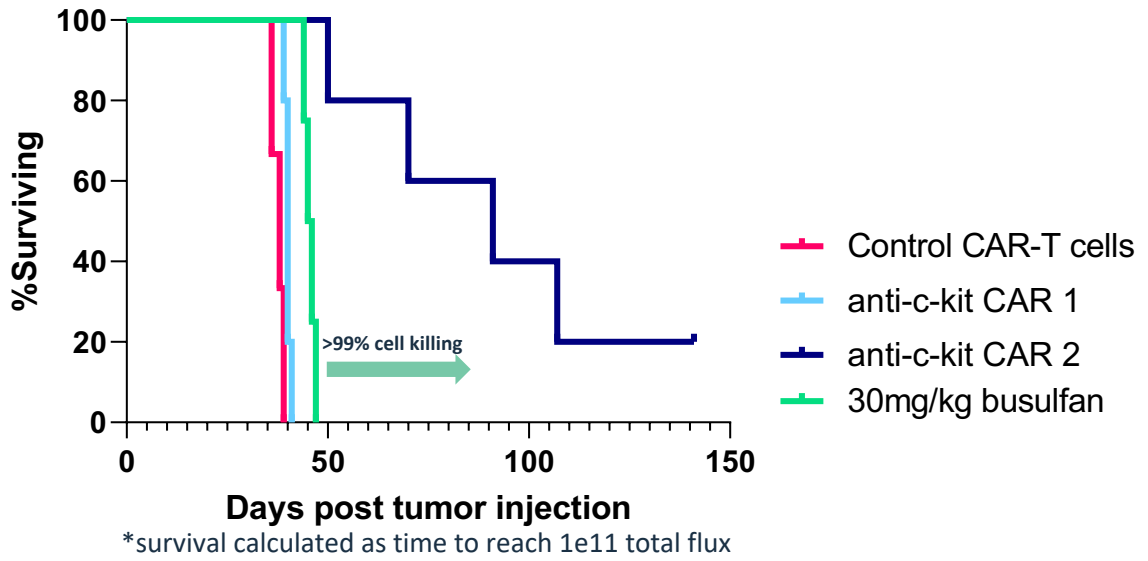


Whole body flux over time



*background BLI in naive mice

Overall Survival*



*survival calculated as time to reach 1e11 total flux

Anti-c-kit CAR-T cells clear Nomo-1 disseminated disease, including upon tumor rechallenge more than 100 days post-transplant, and significantly prolong survival compared to benchmark busulfan treatment

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Summary

- Safer, non-genotoxic conditioning regimens may reduce transplant morbidity and mortality, resulting in better outcomes and a greatly expanded number of potential indications
- Poseida's unique allogeneic CAR-T platform is ideally suited for development as a next generation conditioning agent
- Preliminary *in vivo* experiments have demonstrated the ability of anti-c-Kit CAR-T cells to deplete human stem cell grafts in NSG mice and to prolong survival in a mouse model of AML
- On-going studies continue to evaluate and improve our anti-c-kit CAR-T cell *in vivo* efficacy against AML while developing their use as a conditioning agent in a full transplant model