Lymph Node Targeted Boosting with Cognate Amphiphile-Peptide Vaccines Enhances TCR-T Cell Therapy to Eradicate Solid Tumors

Dylan J. Drakes[1], Abdulraouf Abbas[1], Jacqueline Shields[1], and Peter C. DeMuth[1]

[1] Elicio Therapeutics, Inc. One Kendall Square, Building 1400W, 14303, Cambridge, MA 02139

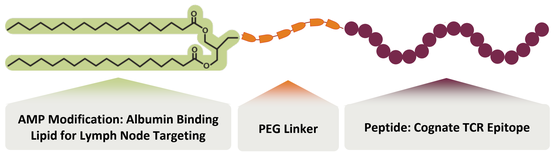
Overview

Clinical results from TCR-T Cell therapies demonstrate anti-tumor efficacy, although therapeutic benefits remain transient due to suboptimal T Cell functional persistence and tumor infiltration alongside antigen escape mechanisms. Amphiphile (AMP) vaccines improve lymph node targeting of cancer immunogens, stimulating an enhanced endogenous anti-tumor response. We describe an approach to generate robust and durable anti-tumor responses by combining AMP lymphatic targeting with TCR-T Cell therapy. AMP cognate peptides traffic to lymph nodes and improve TCR-T Cell activation, persistence, and function compared to soluble (SOL) peptide vaccination or TCR-T Cells alone, inducing a superior anti-tumor effect.

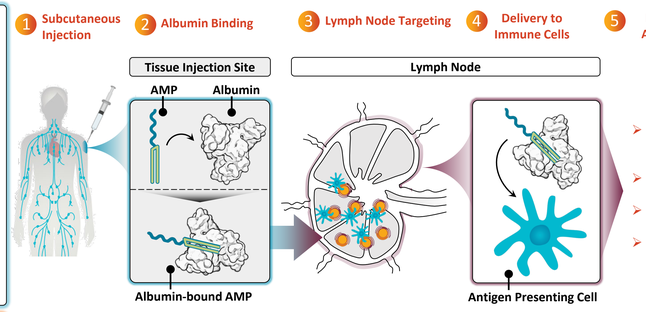
The AMP Platform – Designing a Lymph Node Targeted TCR-T Cell Therapy Booster

AMP-Peptide : Peptide Antigen

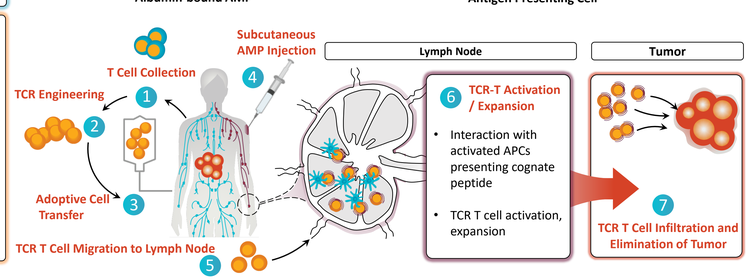
- Cognate peptide target for cancer antigen-specific TCR
- AMP modification gives >10-fold improved lymph node targeting



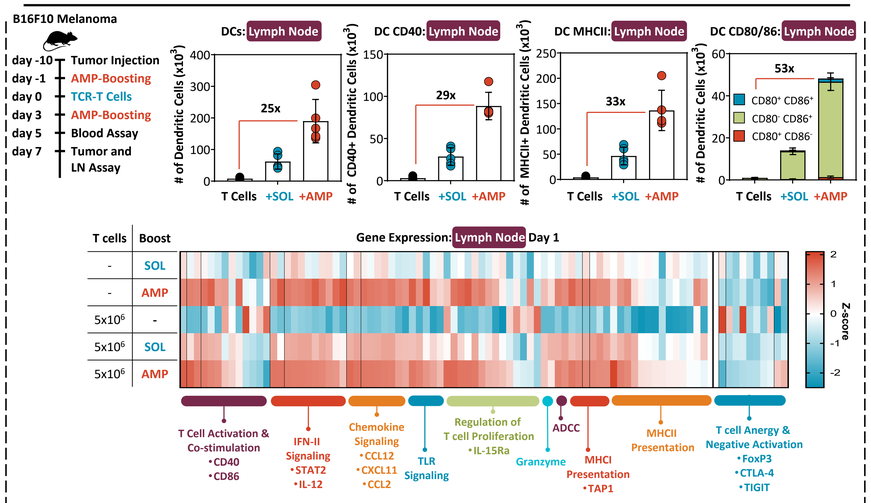
AMP Mechanism: Lymph Node Targeting *via* Albumin Hitchhiking



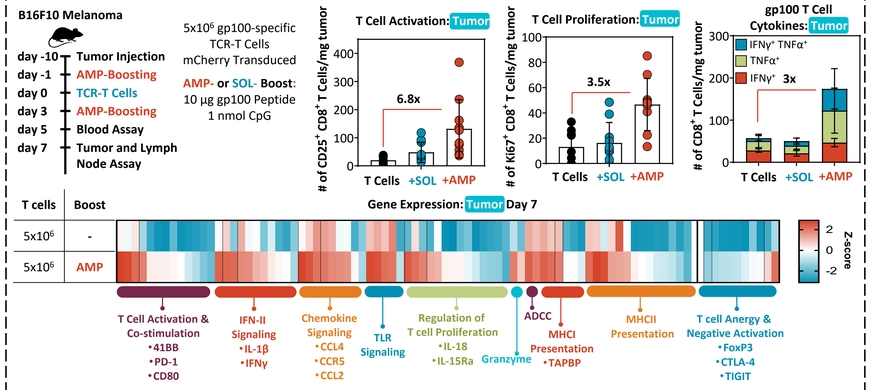
AMP Boosting of TCR-T Cell Therapy:



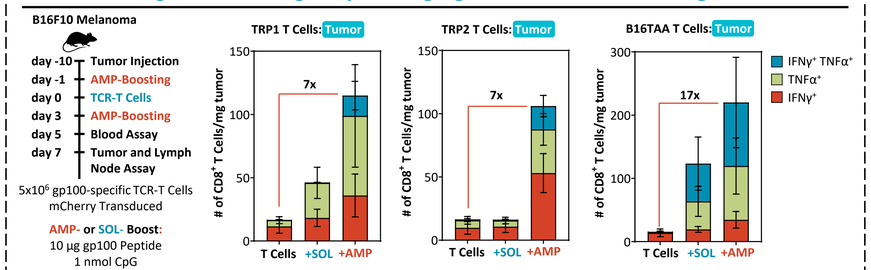
AMP-Boosting Induces DC Activation and Inflammation in Lymph Nodes



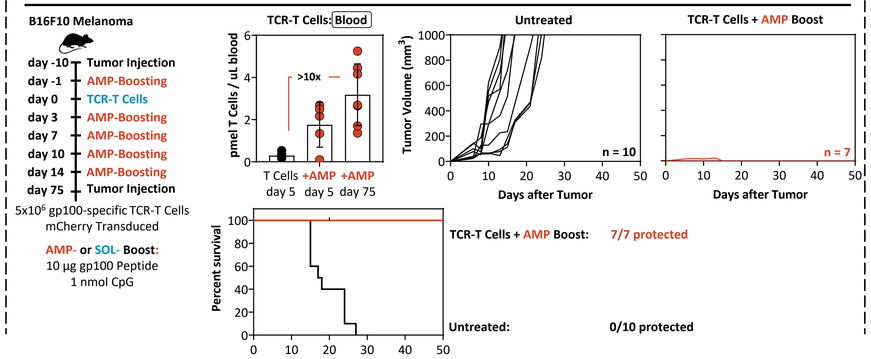
AMP-Boosting Enhances TCR-T Cell Functionality, Proliferation, Activation in the TME



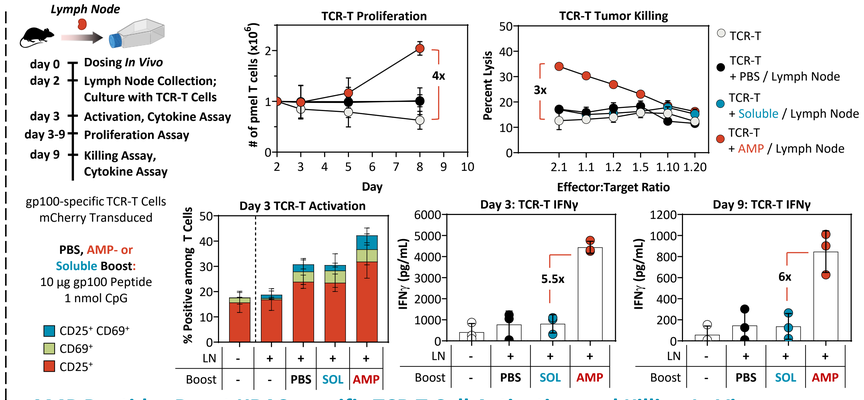
AMP-Boosting Induces Antigen Spreading Against Diverse Tumor Targets



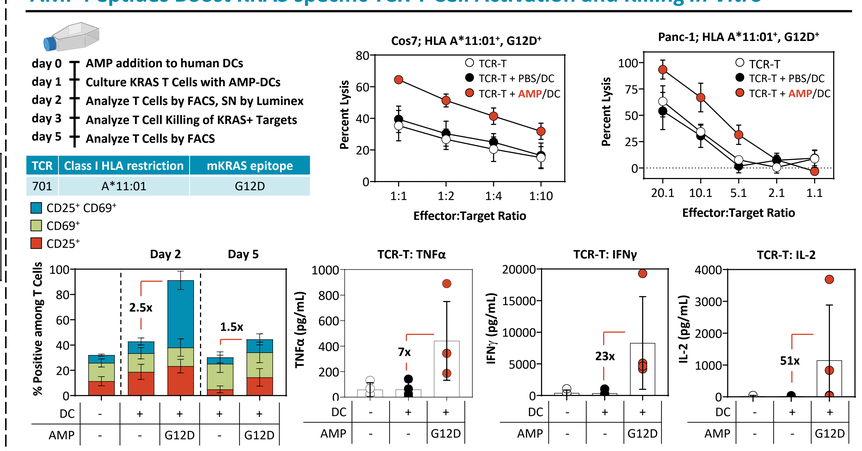
AMP-Boosting Induces Durable TCR-T Cell Responses, Protection Against Rechallenge



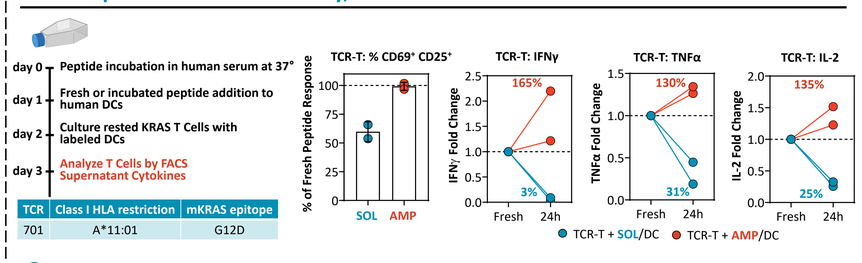
AMP-Boosted Lymph Nodes Enhance TCR-T Proliferation and Function *ex vivo*



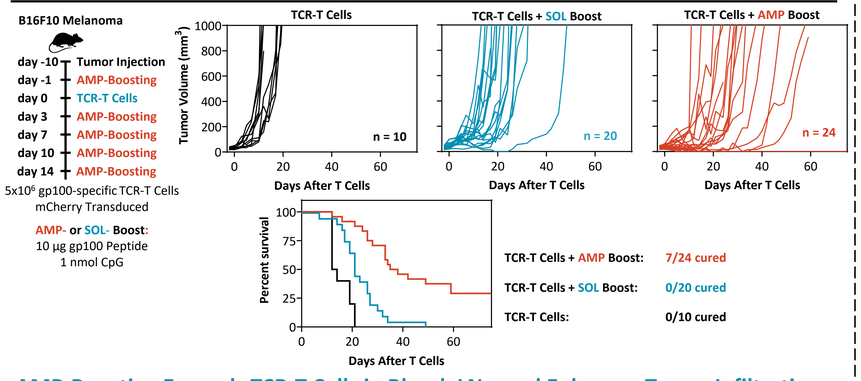
AMP Peptides Boost KRAS specific TCR T Cell Activation and Killing *In Vitro*



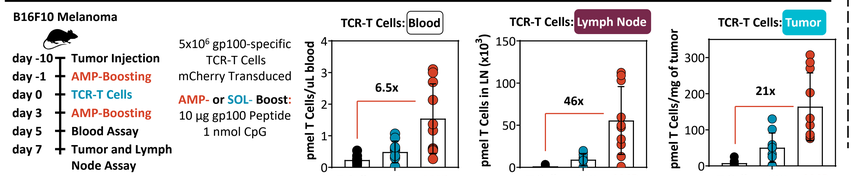
AMP Peptides Maintain Stability, Boost TCR T Cells in Mock *In Vivo* Conditions



AMP-Boosting Enhances TCR-T Therapy to Eradicate Established Solid Tumors



AMP-Boosting Expands TCR-T Cells in Blood, LNs, and Enhances Tumor Infiltration



Summary

- AMP vaccination delivers cognate peptides and adjuvant to lymph nodes which induces DC activation and provides *in vivo* activation of tumor-specific TCR-T Cells to amplify anti-tumor potency of adoptively transferred cells.
- AMP vaccination significantly enhanced TCR-T Cell anti-tumor response and led to durable cures of solid tumors in an established, syngeneic tumor model.
- AMP-peptide pulsed autologous DCs enhanced the function of clinically relevant KRAS-specific TCR-T cells in vitro.
- These studies provide direct rationale and evidence for the combination of AMP vaccination with TCR-T Cell therapies to augment clinical responses.

Acknowledgements

The authors thank Dr. James Yang, M.D. (NCI) for reagents and technical expertise.