

TITLE:

Surface-tethered IL-12 improves tumor-specific T cell therapy and enhances inflammatory activity in tumors without inducing systemic toxicities

AUTHORS:

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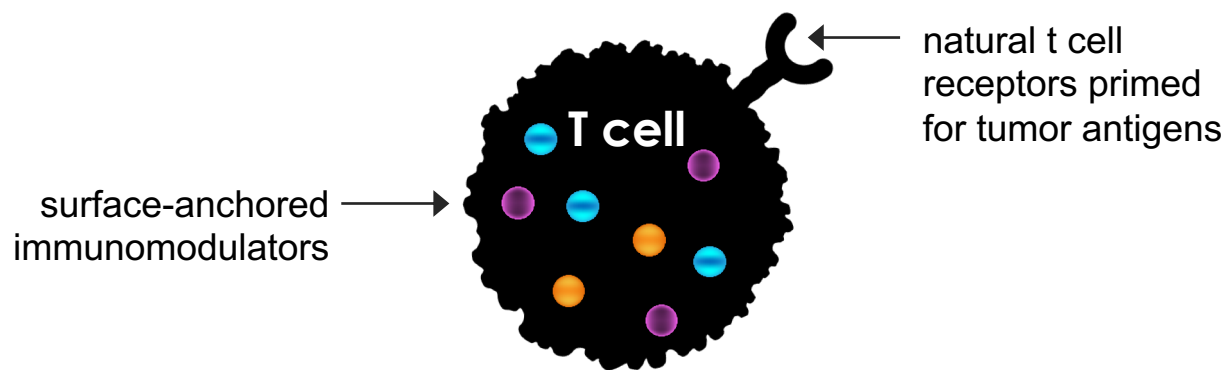
Douglas Jones, PhD
IL-12 Scientific Program Lead
Torque Therapeutics

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Jonathan Fitzgerald
Torque Therapeutics

Torque platform is designed to overcome key cell therapy limitations

Deep-Priming harnesses natural T cell biology



Torque Deep-Primed™ T Cell

Multi-target, antigen-primed T Cells

For efficacy against **heterogeneous tumors**

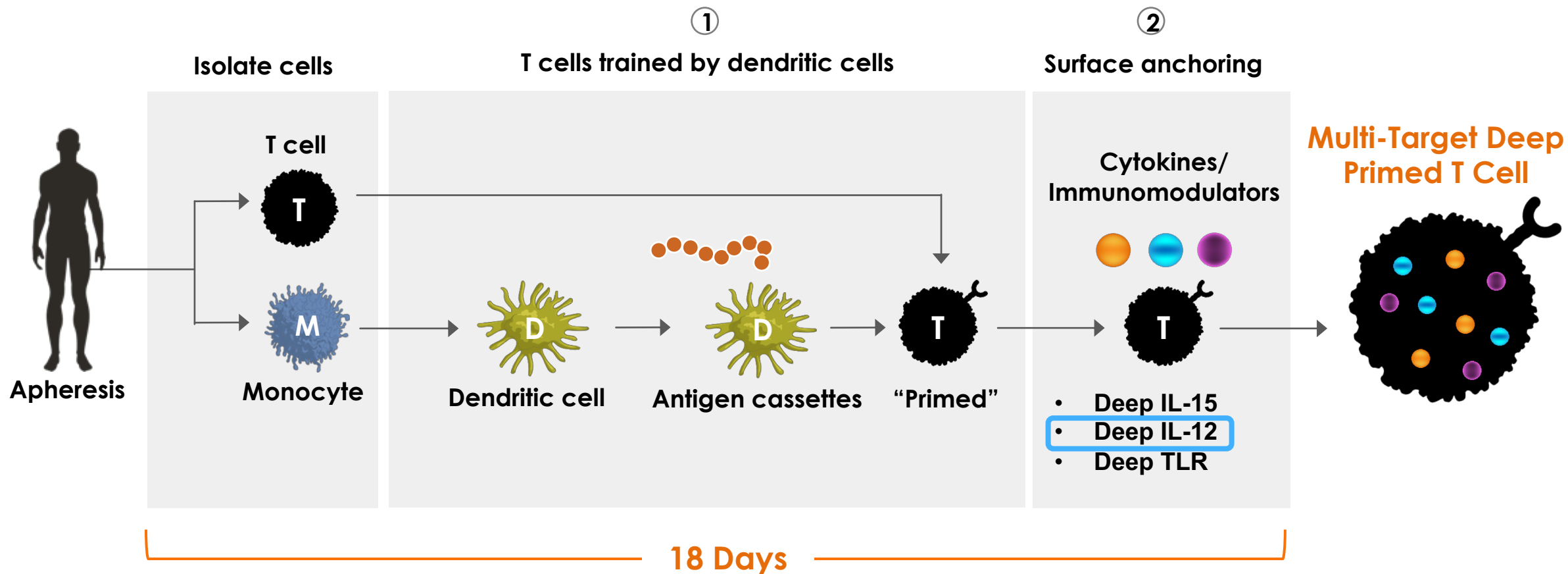
Surface-anchored cytokines / Immunomodulators

To **overcome immunosuppression** in the tumor microenvironment

High margin of safety

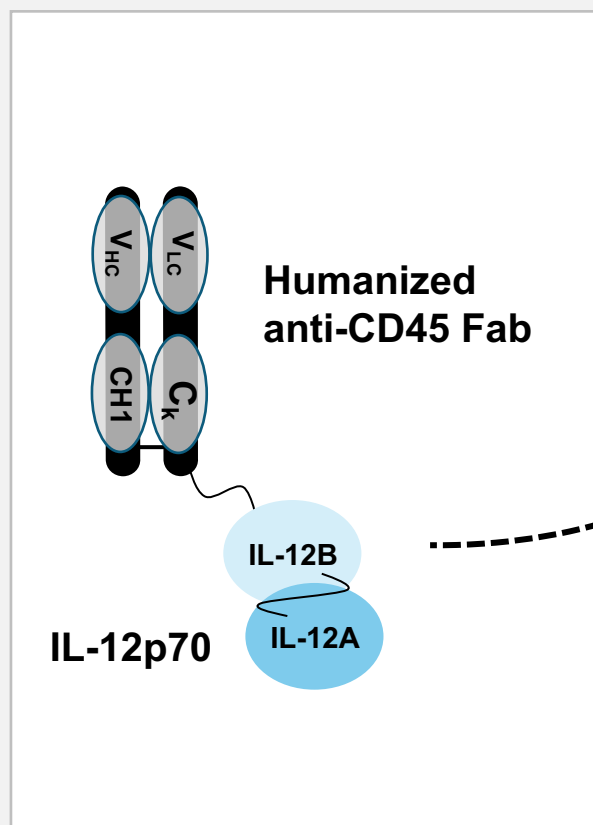
- Outpatient, without myeloablative chemotherapy
- Enables repeat dosing

Torque platform harnesses natural T cell biology with ex vivo process

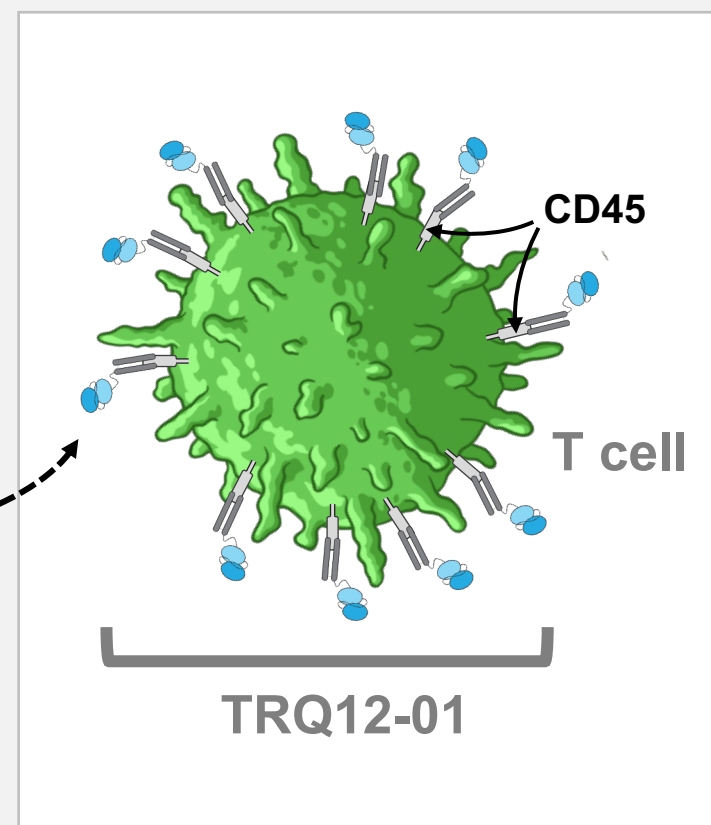


Deep IL-12 delivers controlled dose loading on the T cell surface

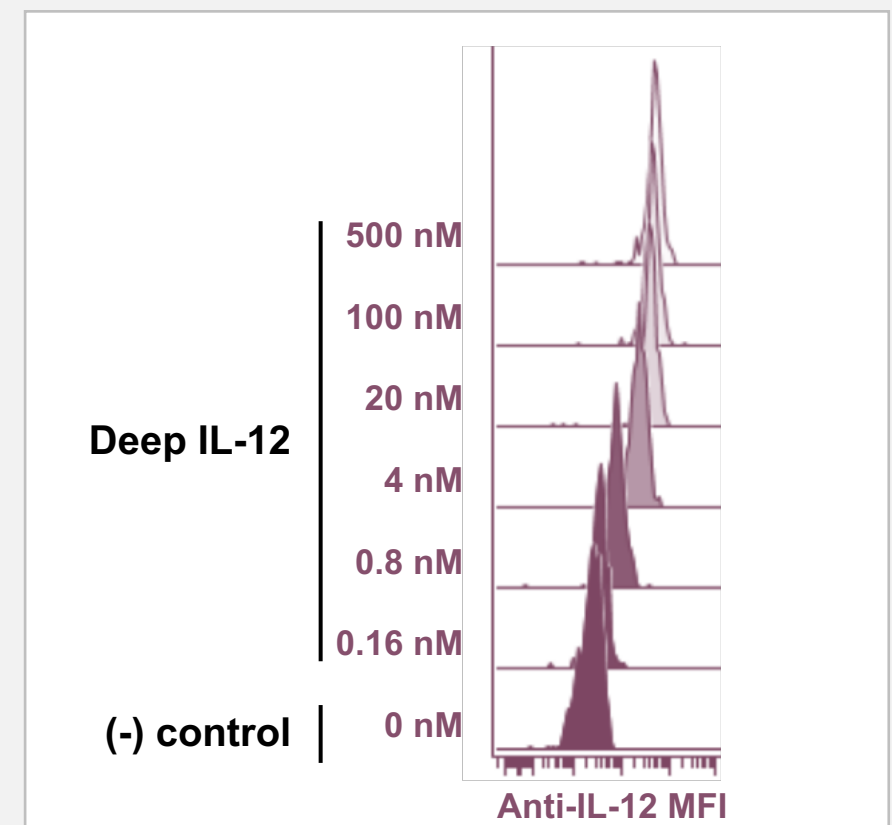
Deep IL-12



Deep IL-12 Primed T cell



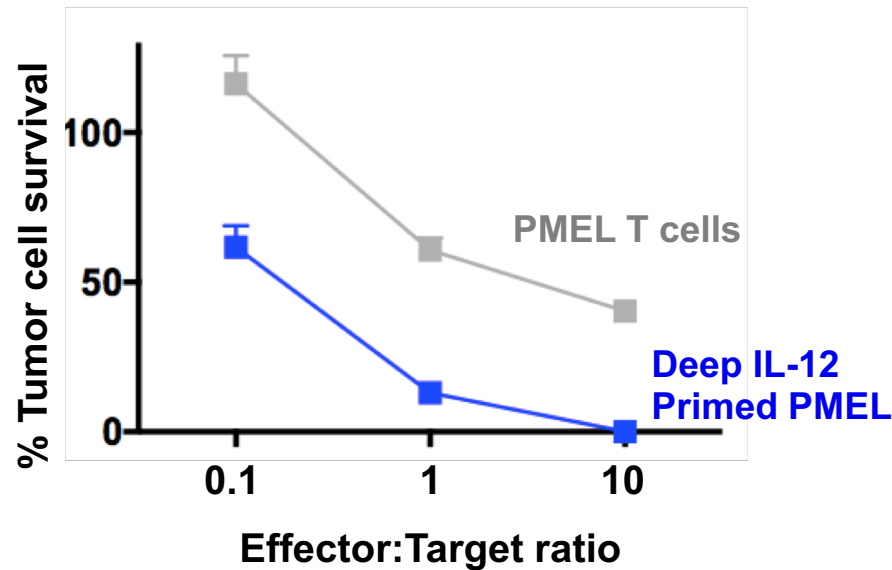
Controlled, uniform IL-12 loading



Cell-tethered Deep IL-12 delivers superior efficacy

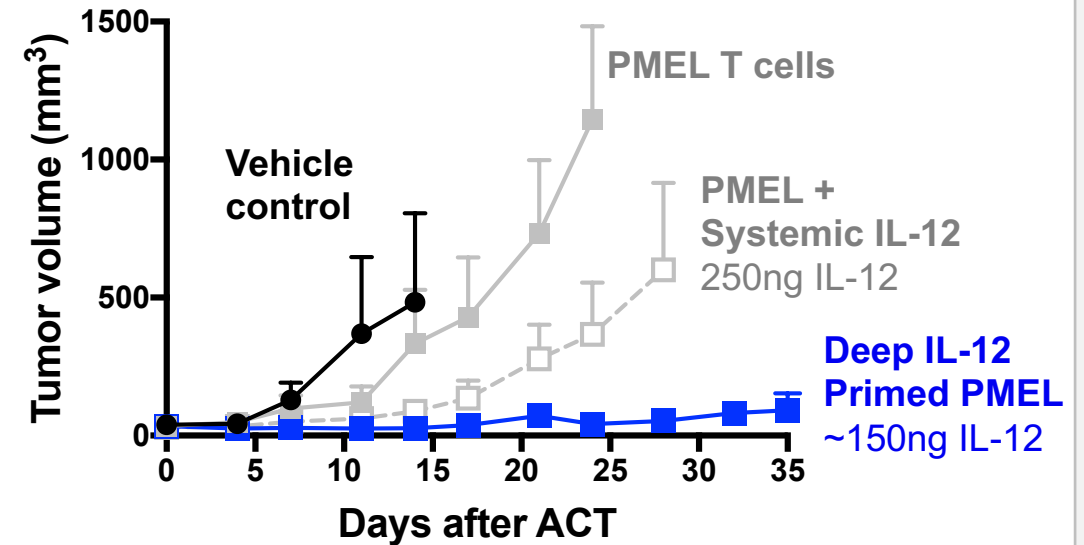
Deeper and more durable response than systemic recombinant IL-12

In vitro cytotoxicity



In vitro B16 melanoma cell killing at 48 hr

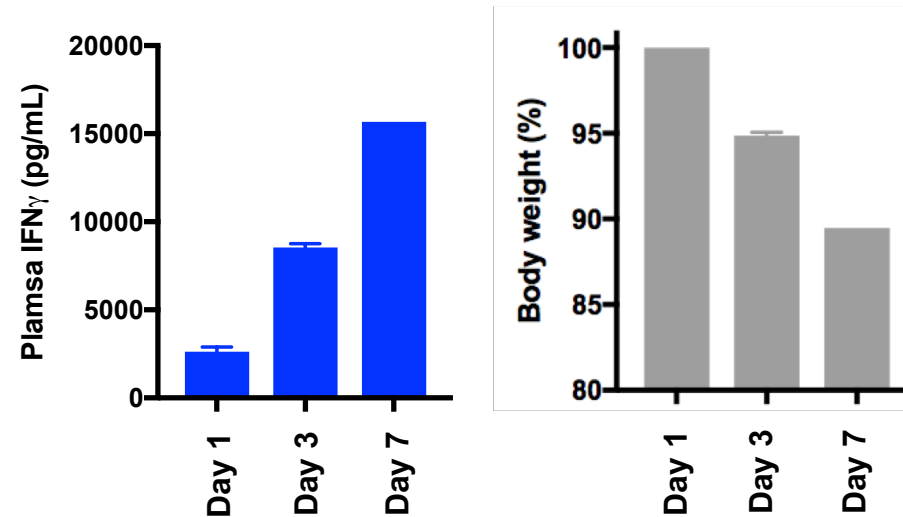
In vivo tumor growth inhibition



PMEL / B16 melanoma tumor model

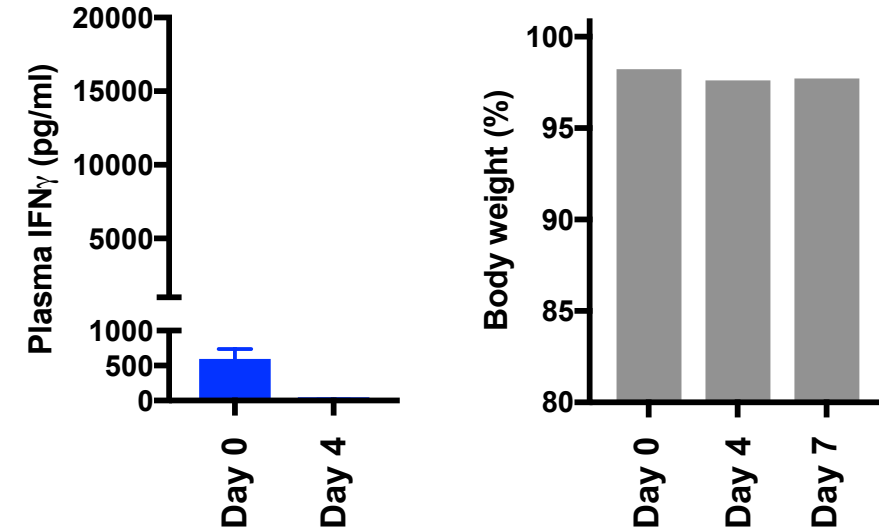
Deep IL-12 delivers favorable systemic profile

Systemic IL-12 IFN γ elevation and systemic toxicities



Daily systemic IL-12
C57BL6

Deep IL-12 Primed T cells Transient circulating IFN γ



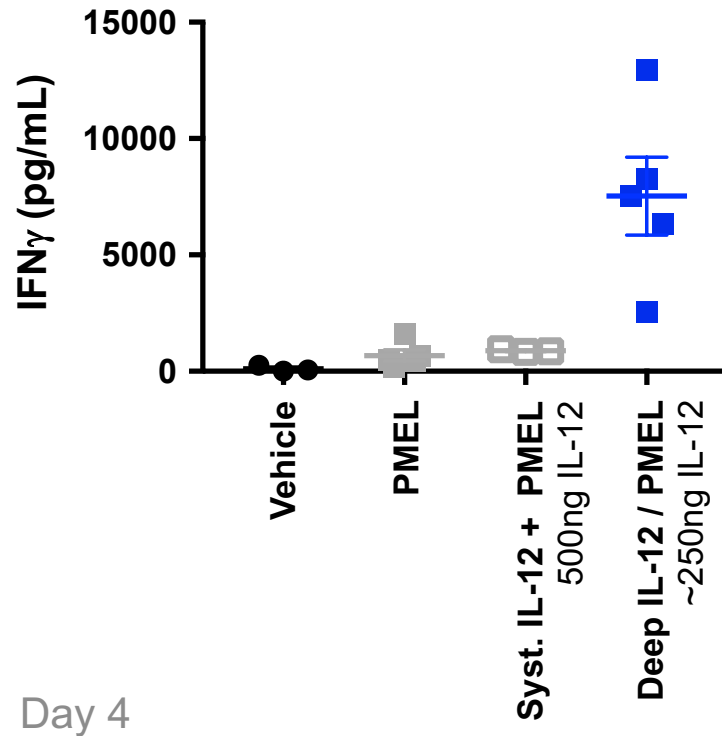
C57BL6

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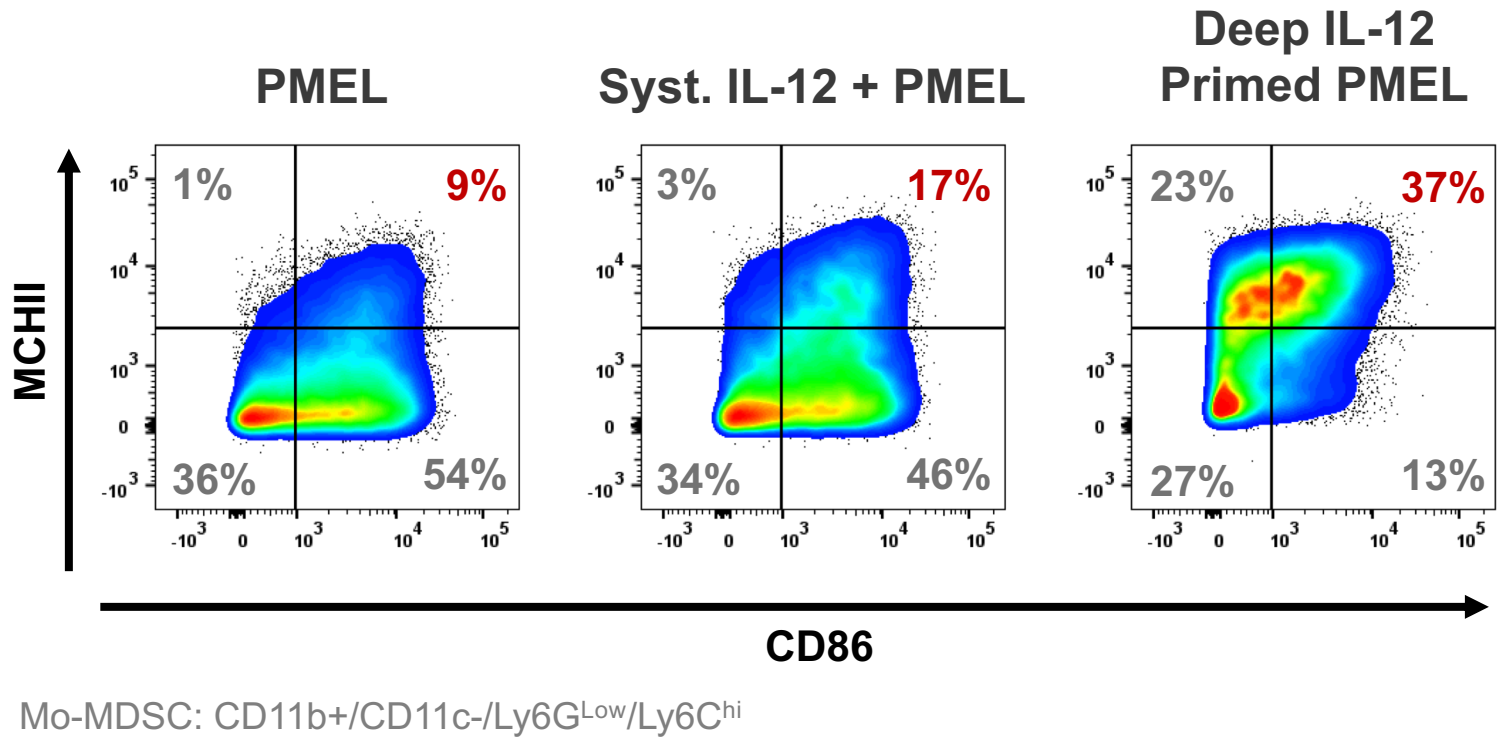
Deep IL-12 induces immune activation in the tumor

Upregulates IFN γ , co-stimulation, and MHC expression

Increased IFN γ production in the tumor



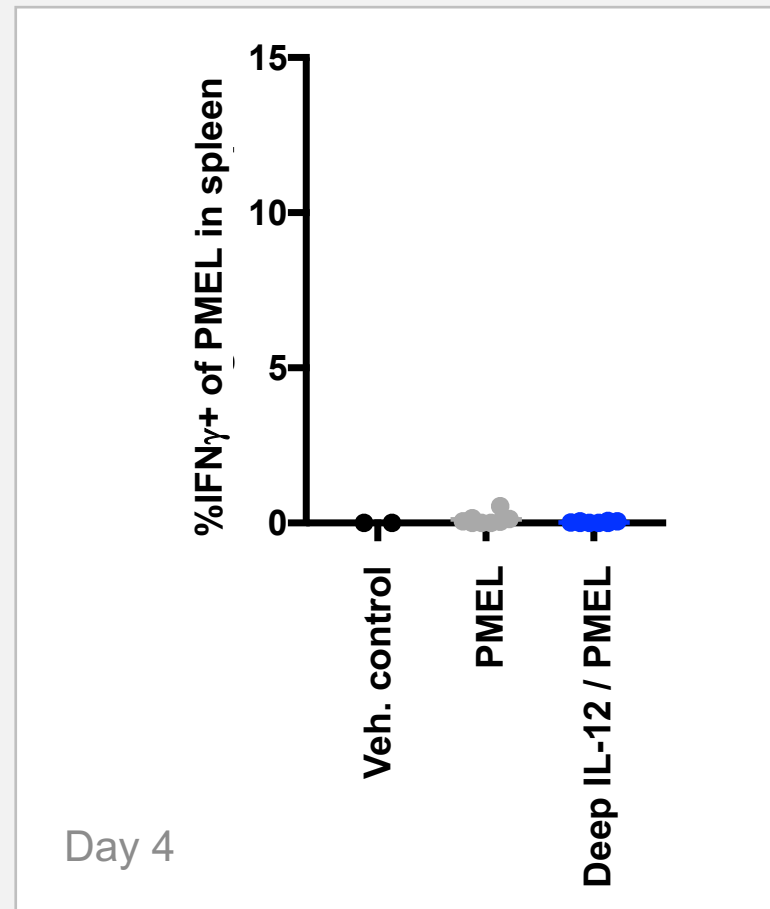
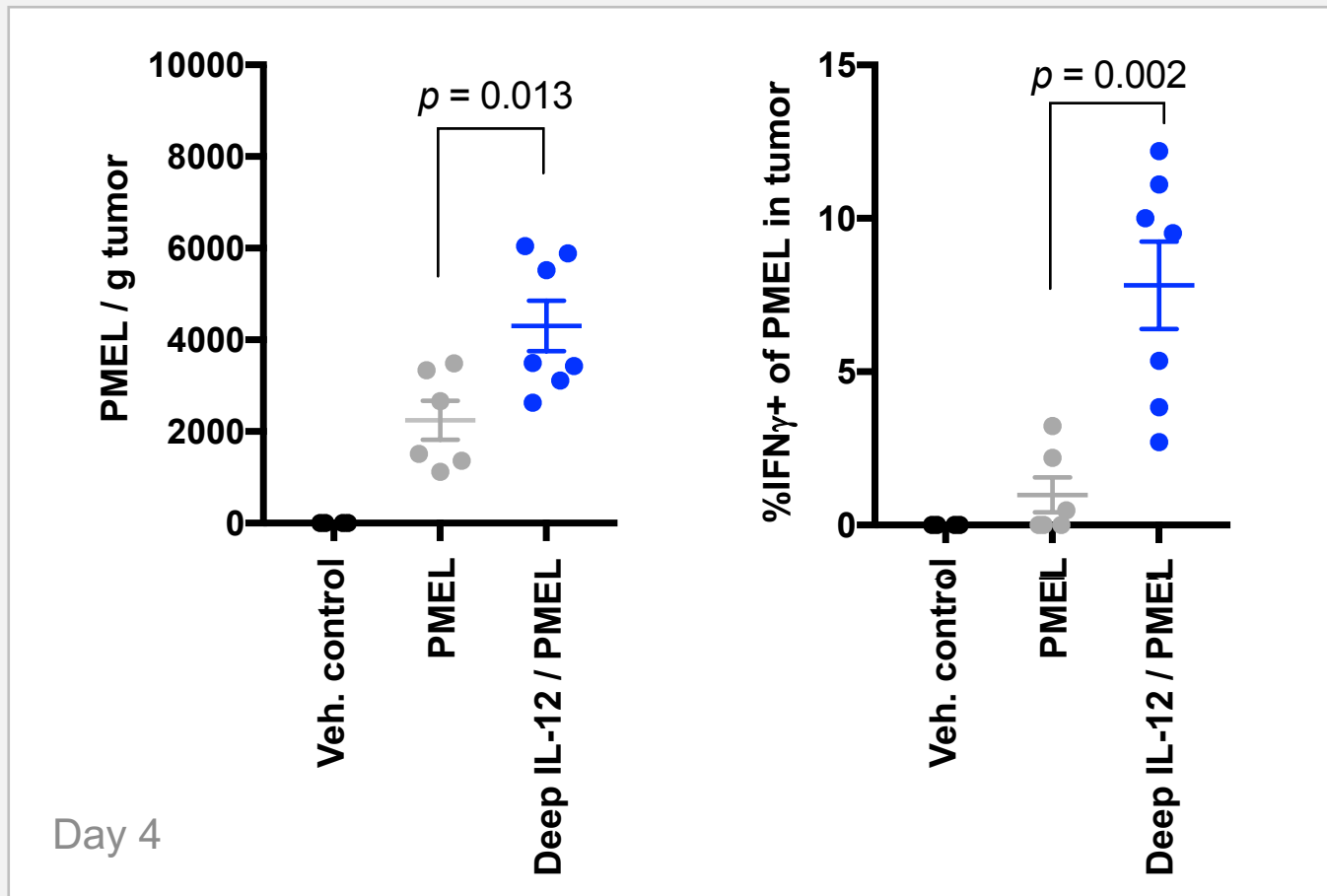
Activating myeloid-derived suppressor cells (Mo-MDSC) in the tumor



Cell-tethered Deep IL-12 drives activity specifically in the tumor

Increased PMEL T cell **expansion and activity** in tumor

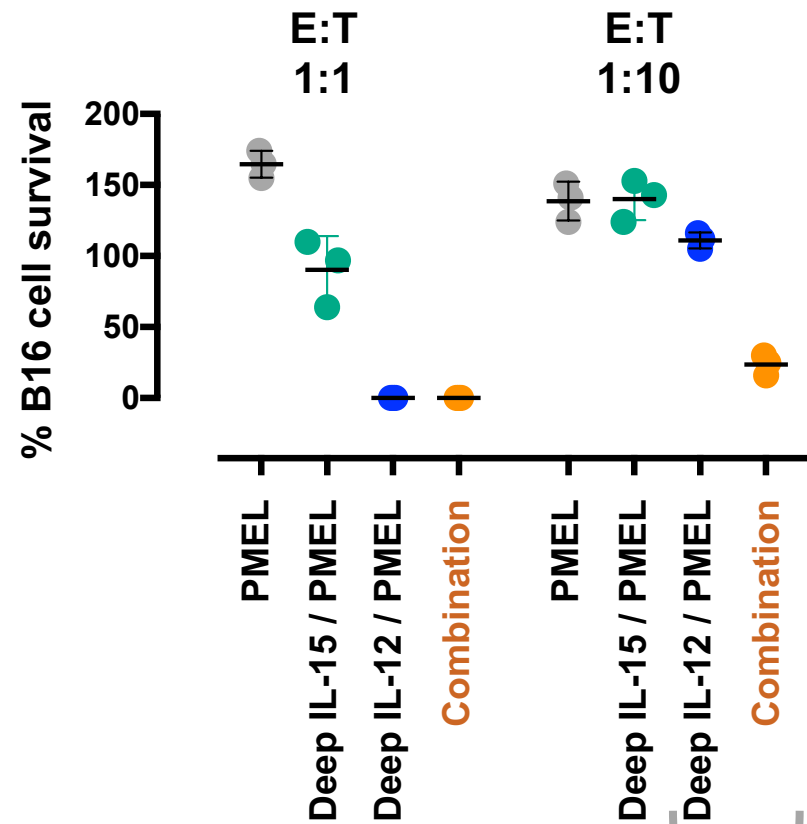
No activity in **spleen**



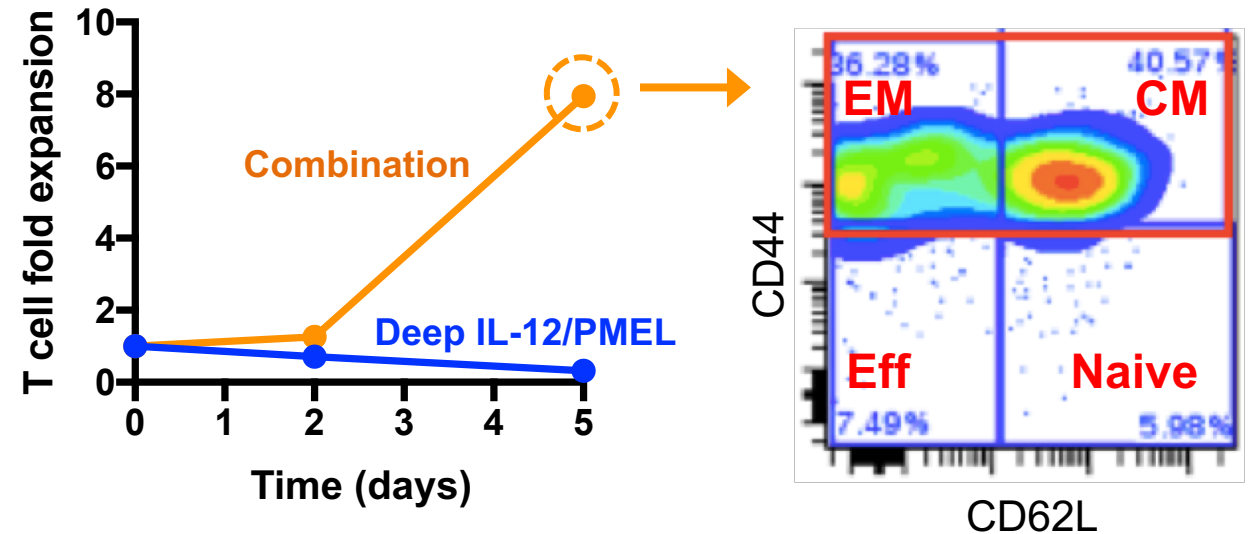
Deep IL-12 and Deep IL-15 combination further enhance T cell activity

Leveraging complementary biology of Deep IL-15 and Deep IL-12

Day 5 cytotoxicity



Memory cell expansion



Torque's Deep Primed T Cell Pipeline

Three Phase 1 Programs in 2019

		ANTIGEN & IMMUNOMODULATOR ↓ COMBINATIONS ↓							UPCOMING MILESTONES
	PRODUCT	IND FILING	ANTIGEN TARGETING	IMMUNOMODULATOR	CHECKPOINT INHIBITOR	LEAD OPTIMIZATION	IND- ENABLING	PHASE 1	
Solid & hematologic tumors	TRQ-1501	✓	Antigen Cassette #1	Deep IL-15					Phase 1 underway
				Deep IL-15	✓				
	TRQ-1502	2019	Antigen Cassette #2	Deep IL-15					Phase 1: 4Q19
				Deep IL-15	✓				
Solid & hematologic tumors	TRQ-1201	2019	Antigen Cassette #1	Deep IL-12					Phase 1: 4Q19
				Deep IL-12 } Combo Deep IL-15 }					
				Deep IL-12 } Combo Deep IL-15 }	✓				
Solid tumors	TRQ-TLR	2020	TBD	Deep TLR					Candidate: 2019

Acknowledgements



Torque Therapeutics

- Gulzar Ahmad, PhD
- De-Kuan Chang, PhD
- Jonathan Nardozzi, PhD
- Kate Sackton, PhD
- Pengpeng Cao, PhD
- Jesse Lyons, PhD
- Karsten Sauer, PhD
- Thomas Andresen, PhD



Technical University of Denmark

APC profiling in TME

- Lars Peterson, PhD
- Ditte Jaegher
- Esben Christensen



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**Deep-Primed™
Cancer Immunotherapy**

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Surface-tethered IL-12 for T cell cancer immunotherapy

AACR Annual Meeting 2019

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