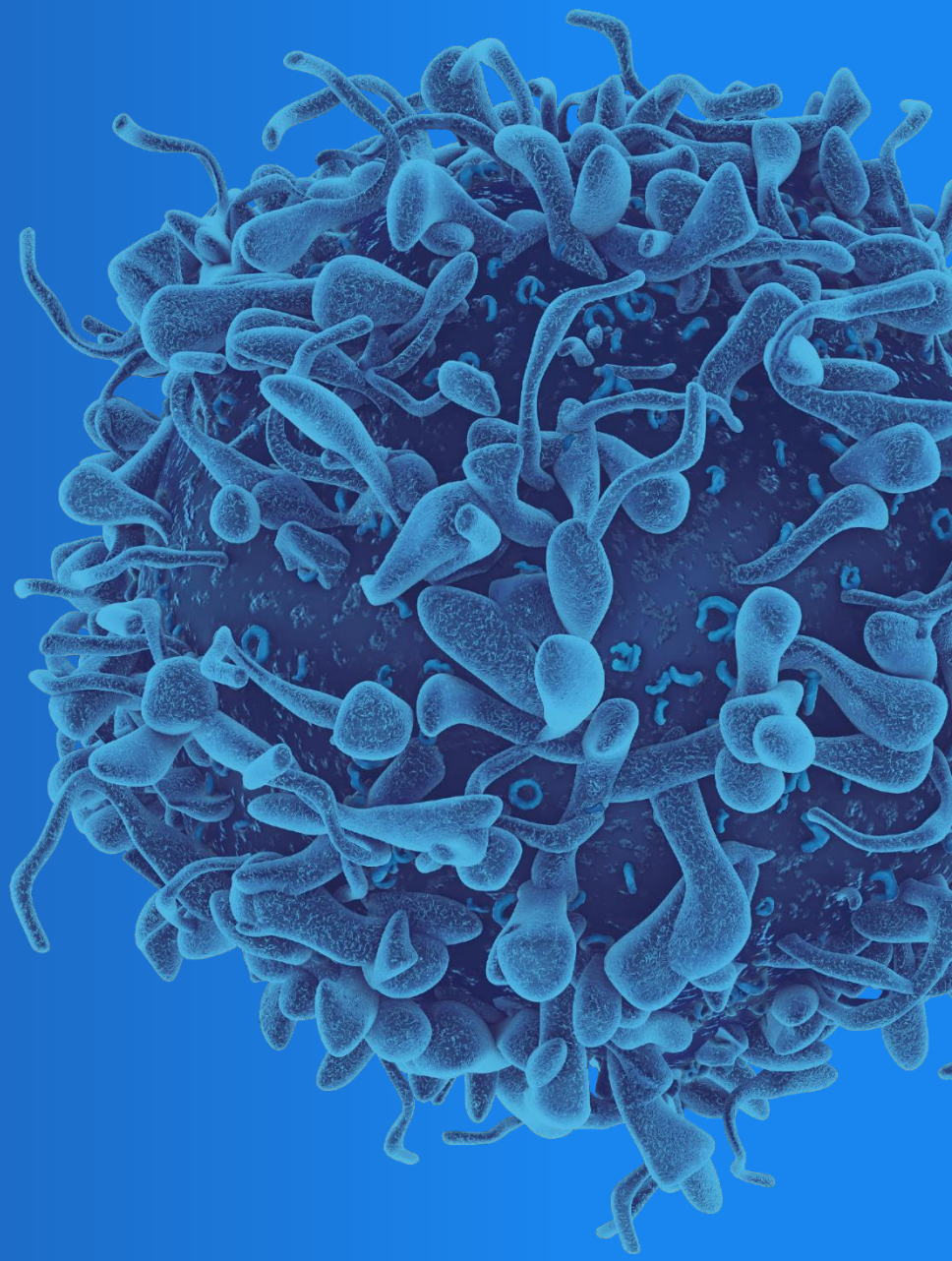
Adicet Bio

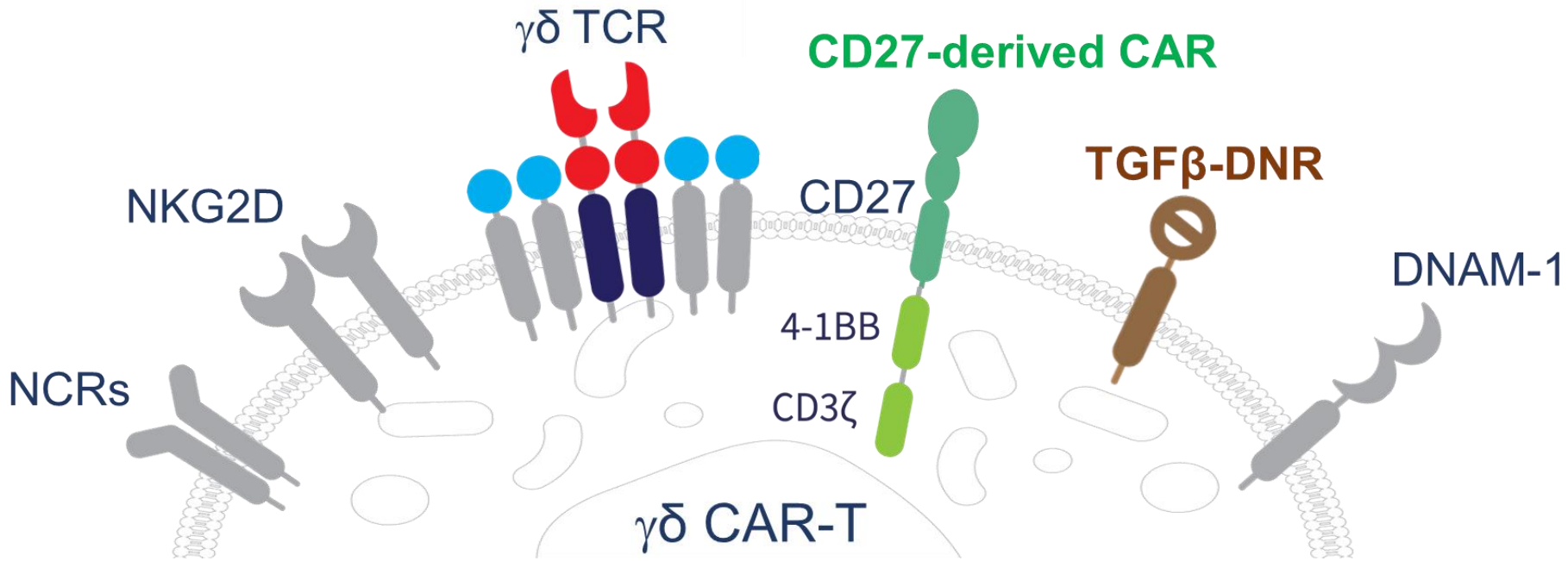
ADI-270: An Armored Allogeneic Anti-CD70 CAR γδ T cell Therapy Candidate Designed for Multiple Solid and Hematological Cancer Indications



Shon Green, PhD
VP, Nonclinical Development

27th ASGCT Annual Meeting 2024
Baltimore, MD

ADI-270: Designed to address multiple refractory cancers



- CAR utilizes CD27 as the binding domain and contains CD27 and 4-1BB costimulatory domains plus CD3ζ (3rd gen)
- Inactive form of TGFβ receptor II to mitigate the immunosuppressive effects of TGFβ within the tumor microenvironment
- Host vs graft armoring against alloreactive activated CD70+ T cells to increase persistence
- Combines endogenous γδ innate and adaptive mechanisms to recognize and kill malignant cells

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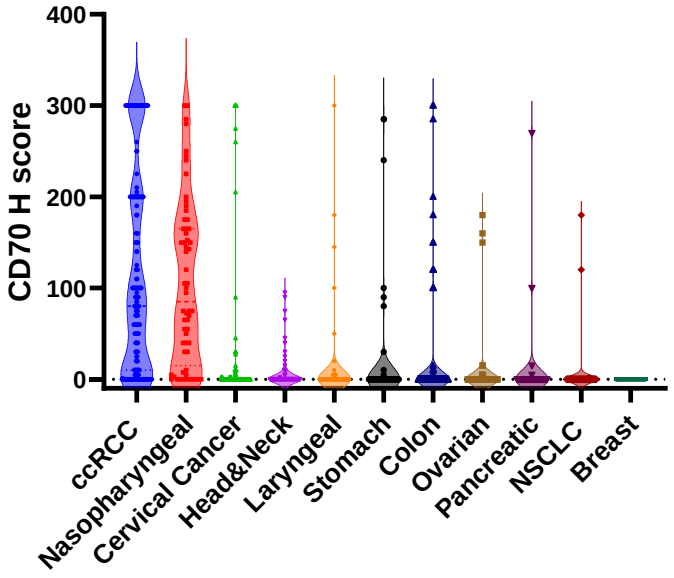
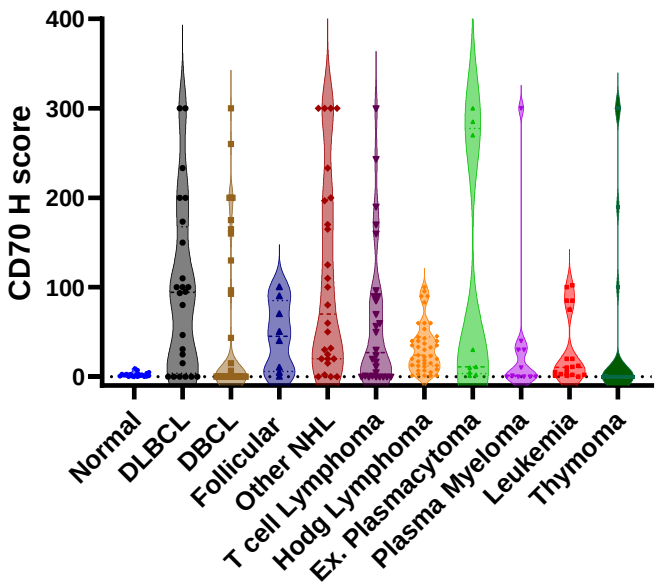
CD70 is expressed on multiple solid and hematological cancers with limited expression in normal tissues

- High expression in multiple solid and heme malignancies
  - Beyond ccRCC and NPC, multiple solid tumors are of interest when paired with CD70 screening
- Minimal expression on normal tissues (activated lymphocytes)
- Target has clinical safety experience

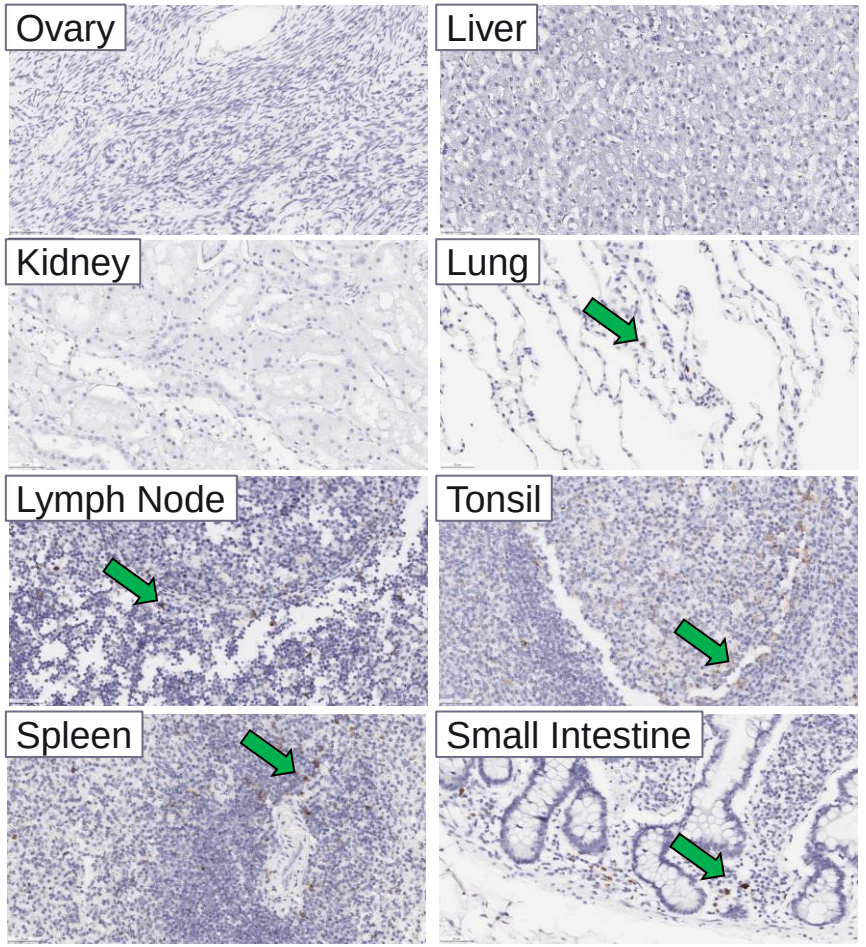
Solid tumors



Hematological malignancies



Representative images from a normal tissue array stained for CD70



Adicet Bio internal data
ccRCC= Clear cell renal cell carcinoma; NPC= Nasopharyngeal carcinoma

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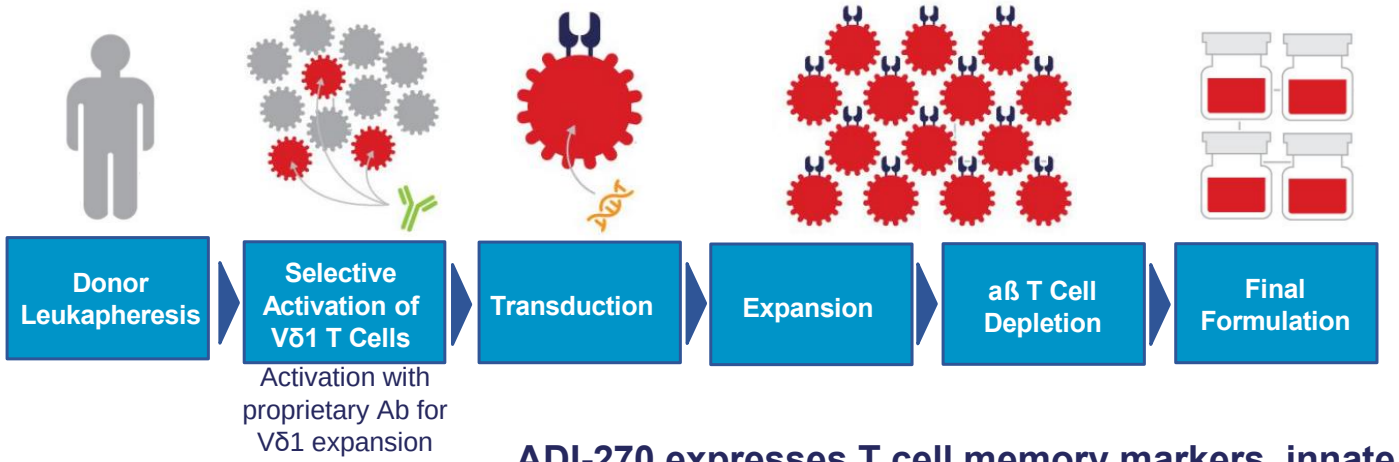
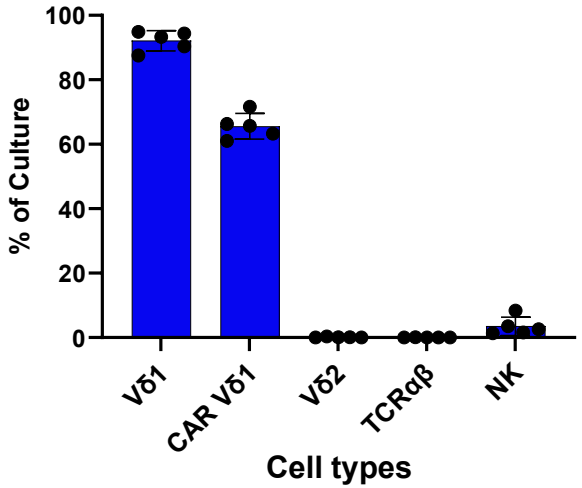
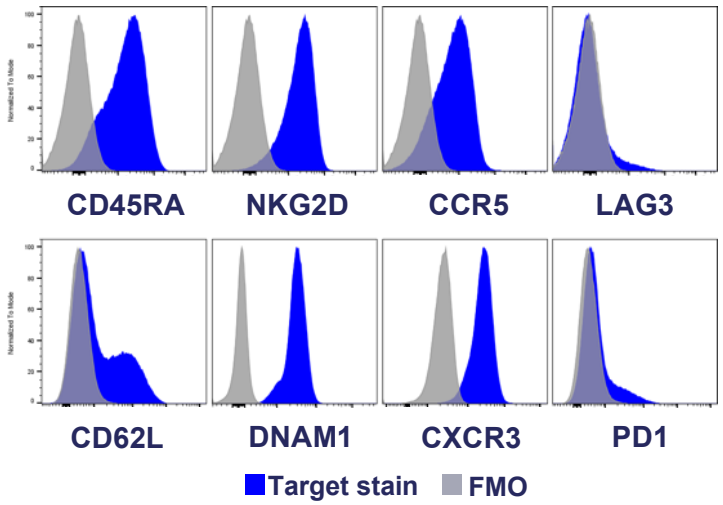
ADI-270 highly enriched for Vδ1 and memory phenotype

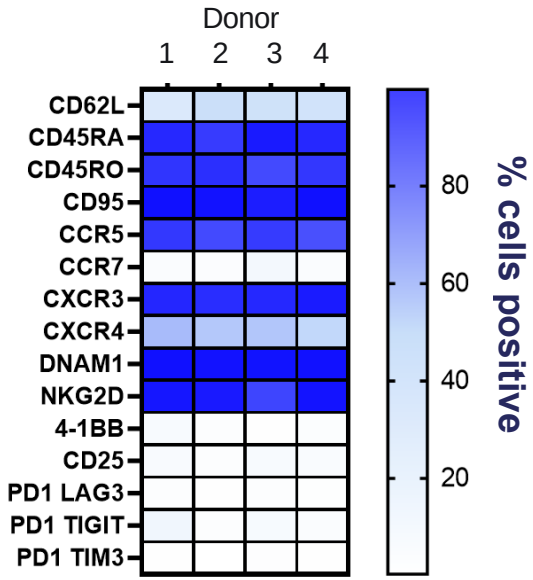


ADI-270 is highly pure for Vδ1 T cells



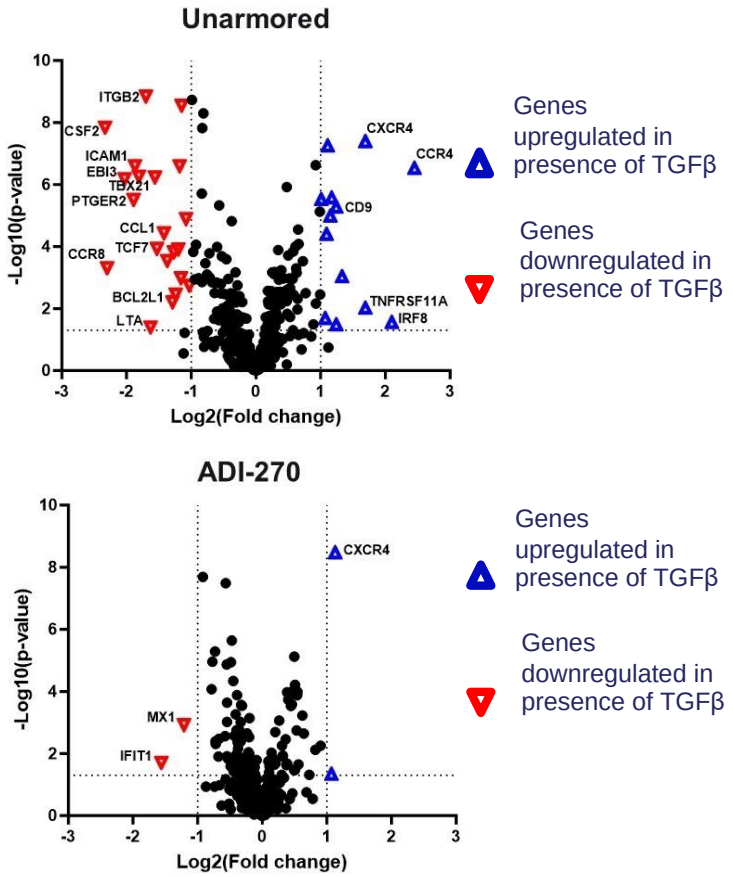
ADI-270 expresses T cell memory markers, innate and chemokine receptors, but largely lacks exhaustion-associated markers

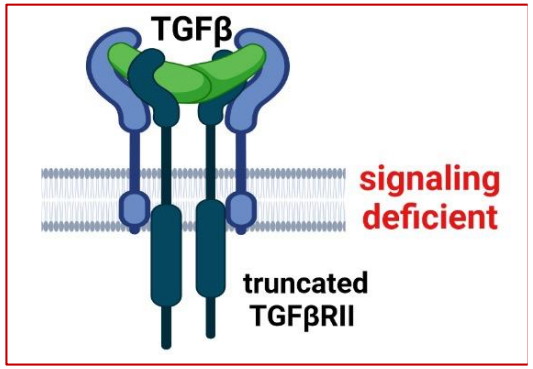




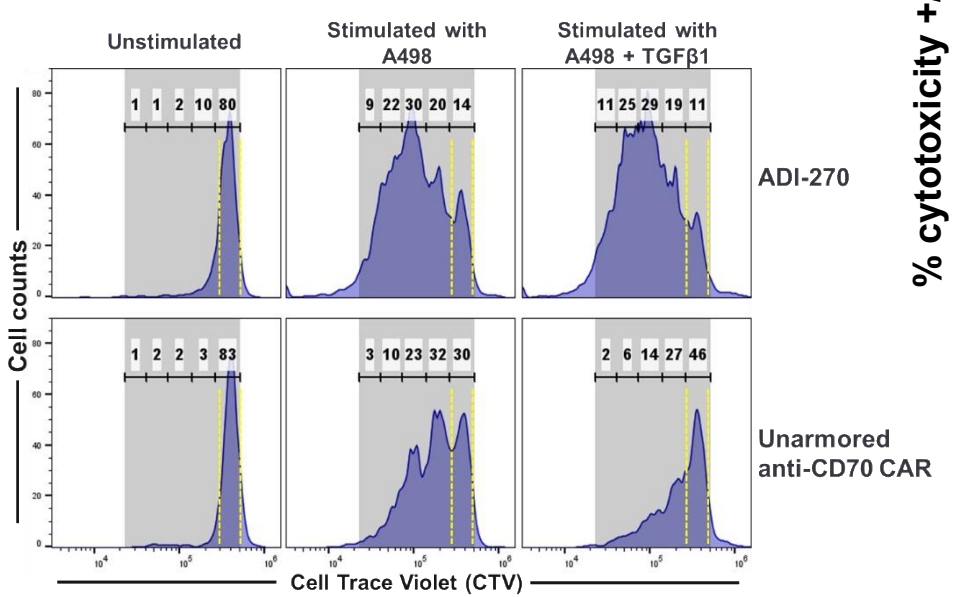
ADI-270 is resilient to the inhibitory effects of TGFβ

ADI-270 showed resilience to transcriptional changes driven by TGFβ signaling

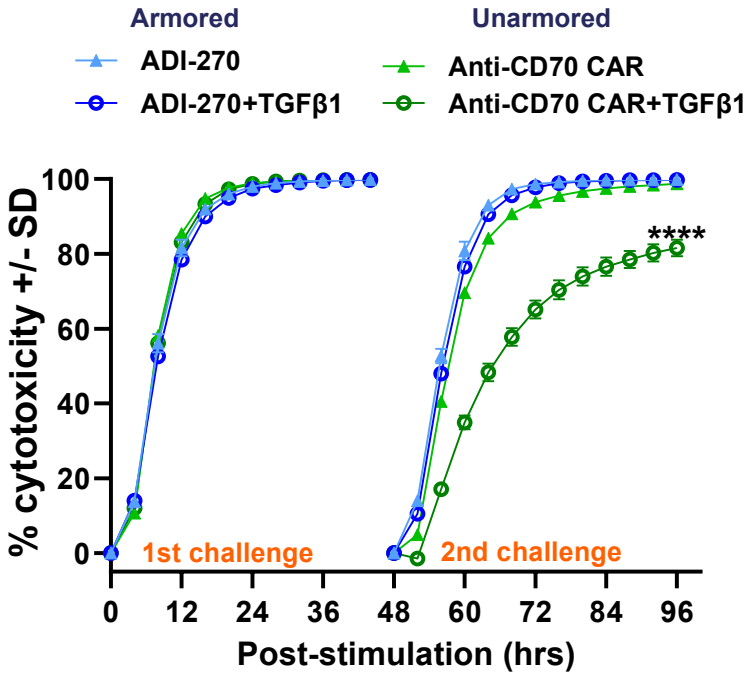




ADI-270 maintained proliferation in the presence of TGFβ

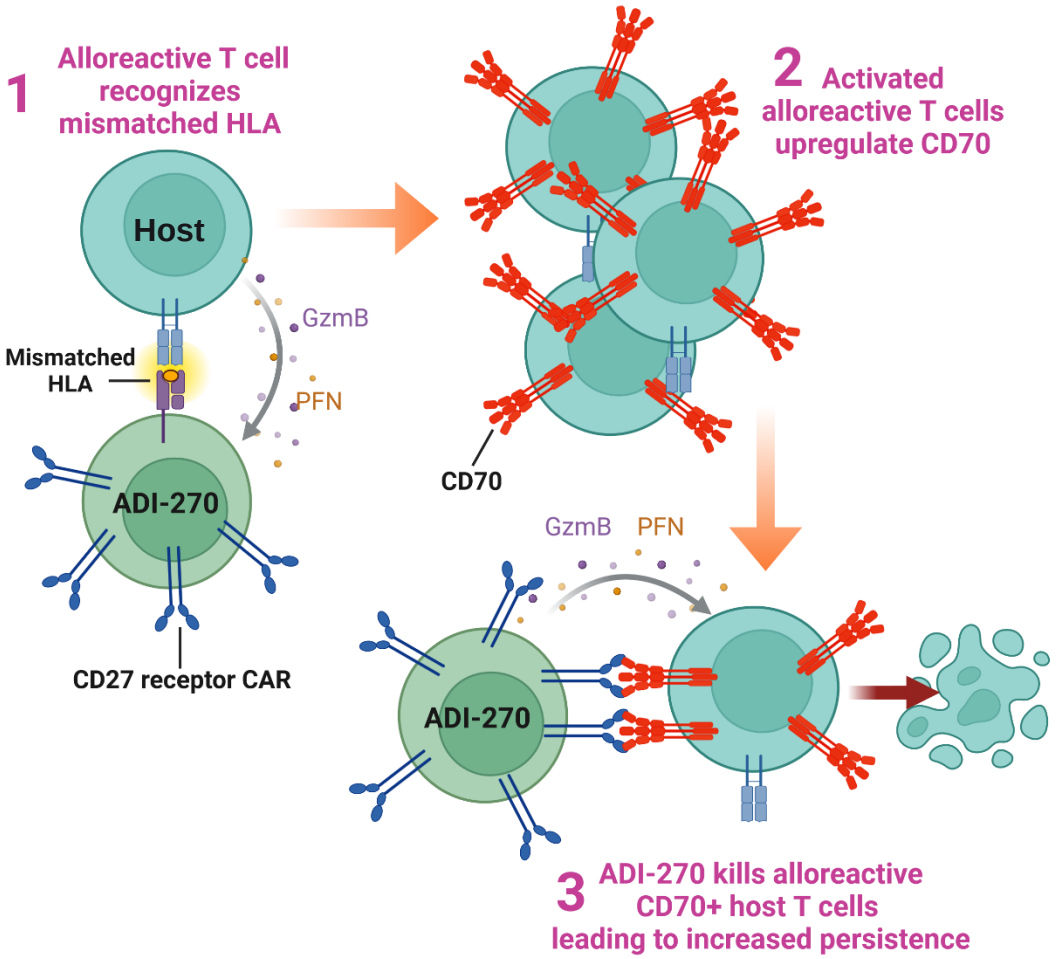


ADI-270 maintained cytotoxicity in the presence of TGFβ

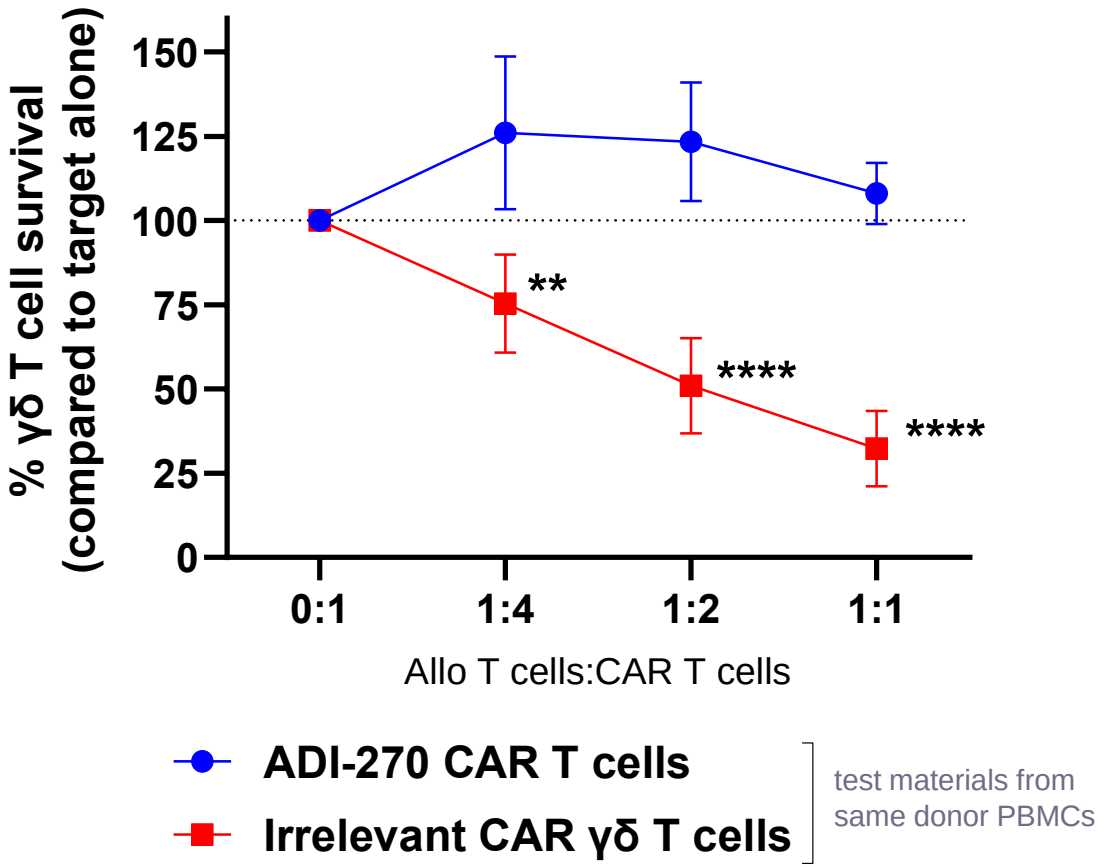


CD70-targeting armors ADI-270 against alloreactive host T cells

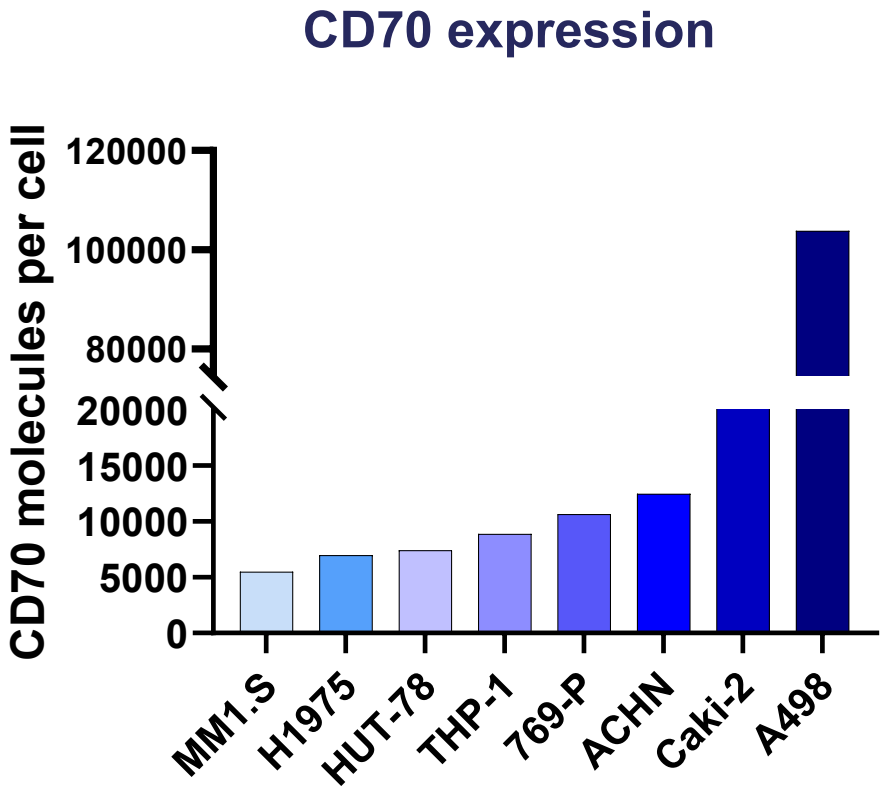
Proposed MoA for enhanced persistence of ADI-270

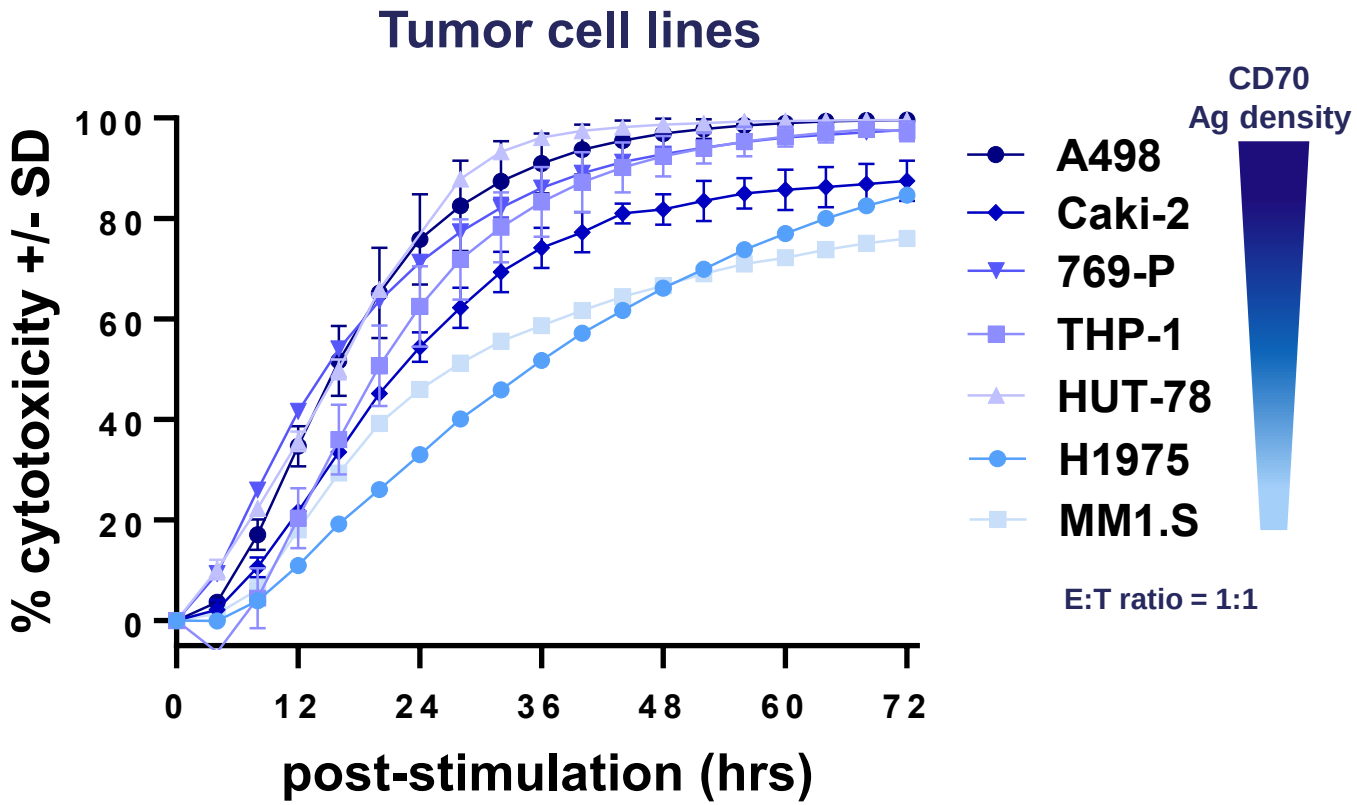


ADI-270 persisted in culture with primed alloreactive T cells derived from 3 donors



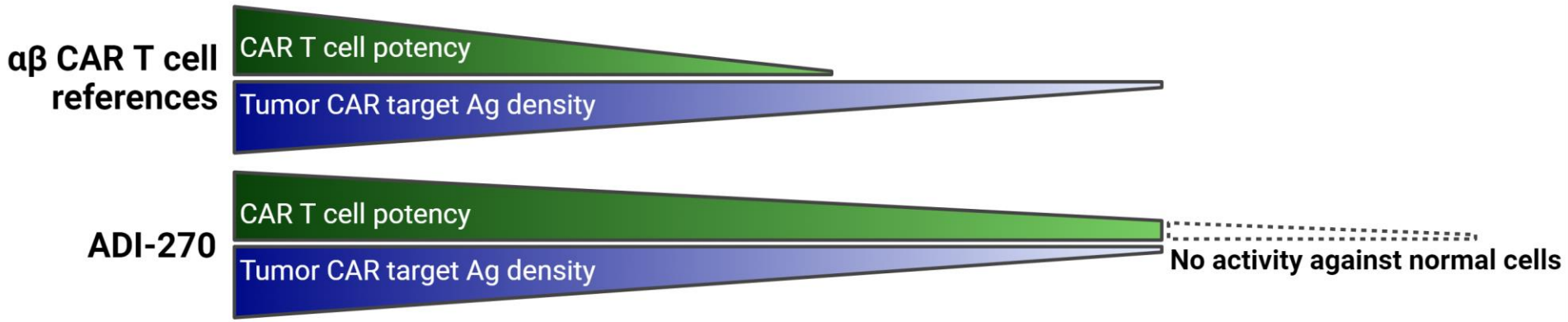
ADI-270 exhibited potent in vitro cytotoxicity against a range of CD70 levels in a diverse set of solid and heme malignancies

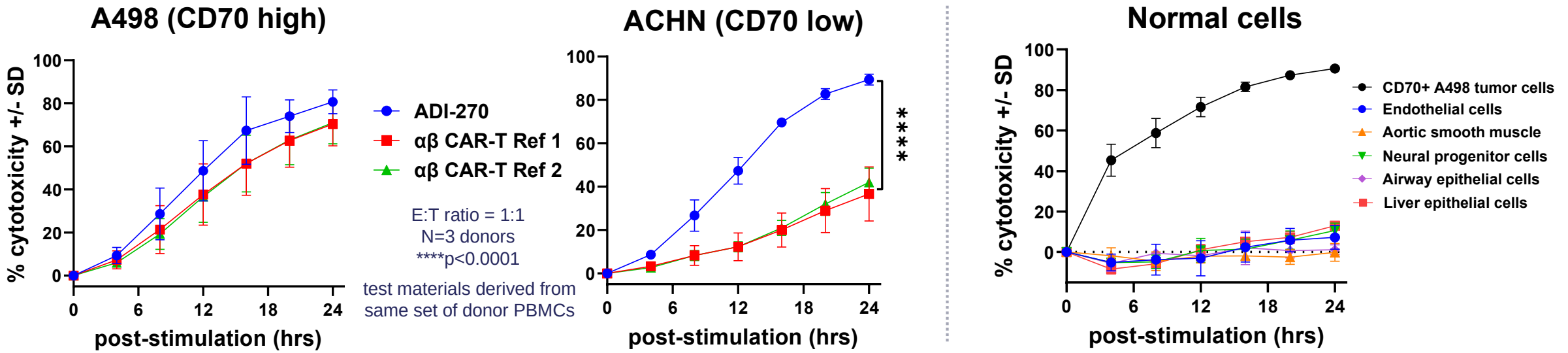




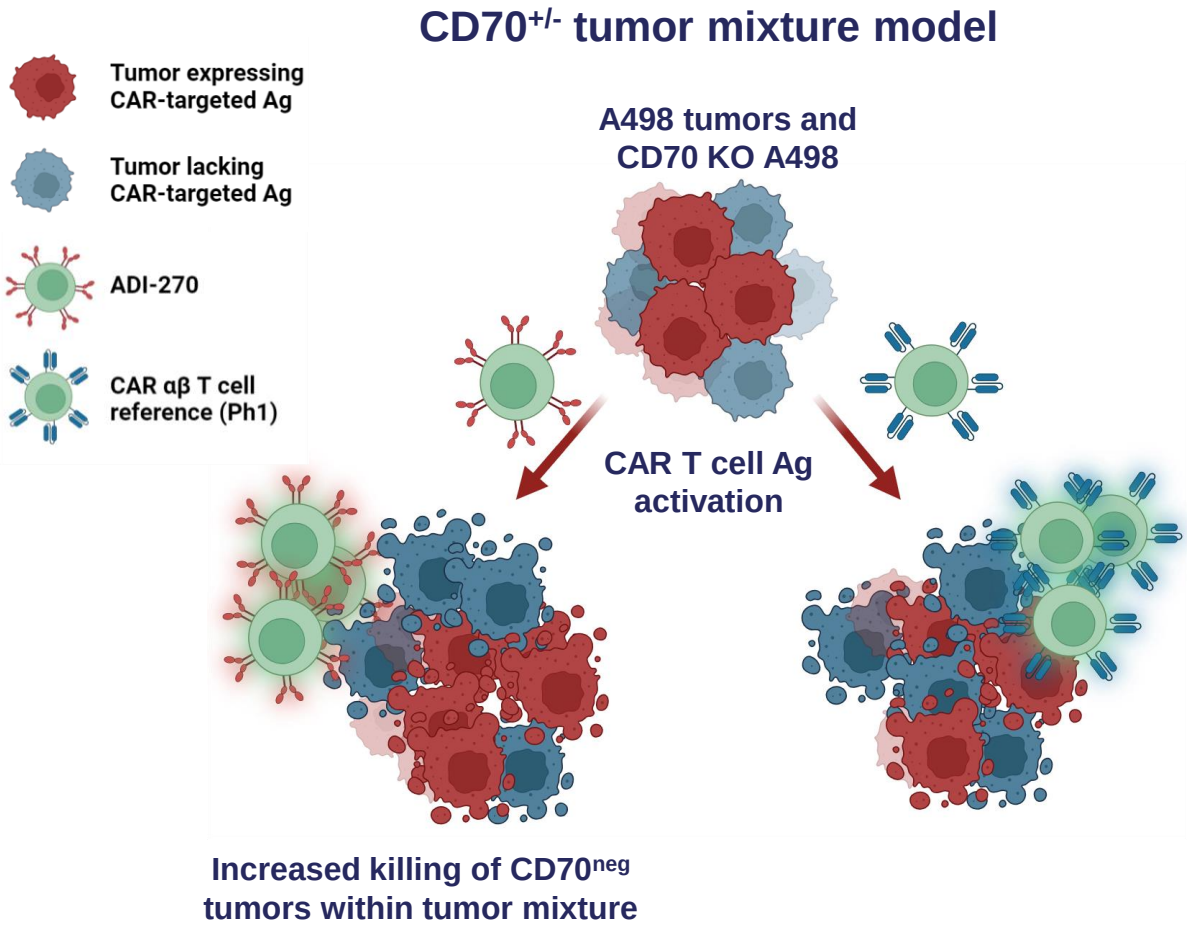
A498, Caki-2, ACHN, 769-P	Renal Cell Carcinoma
THP-1	Acute Lymphoblastic Leukemia
HUT-78	Cutaneous T cell lymphoma
H1975	Non-small cell lung cancer
MM1.S	Multiple Myeloma

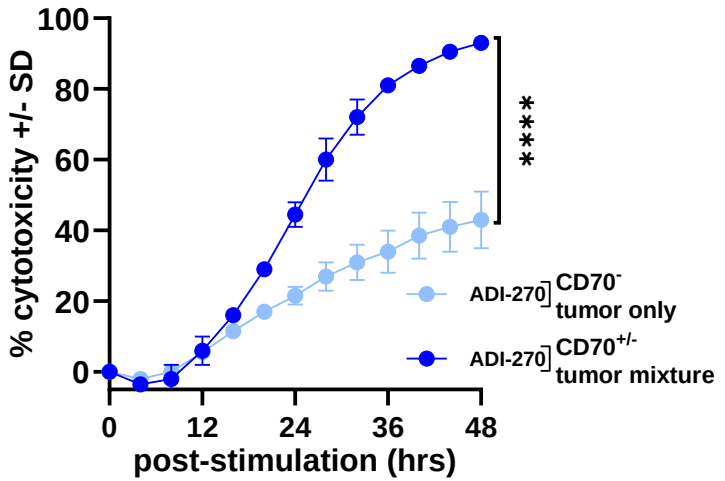
ADI-270 retained potent activity in the context of CD70-low tumors compared to clinically relevant CD70-targeting αβ CAR T cell benchmarks

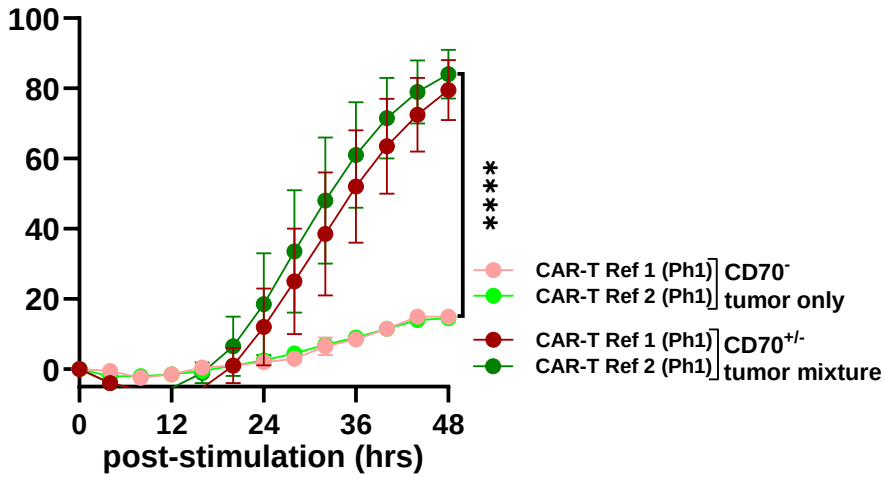




ADI-270 contributed CAR-dependent and CAR-independent mechanisms of tumor targeting



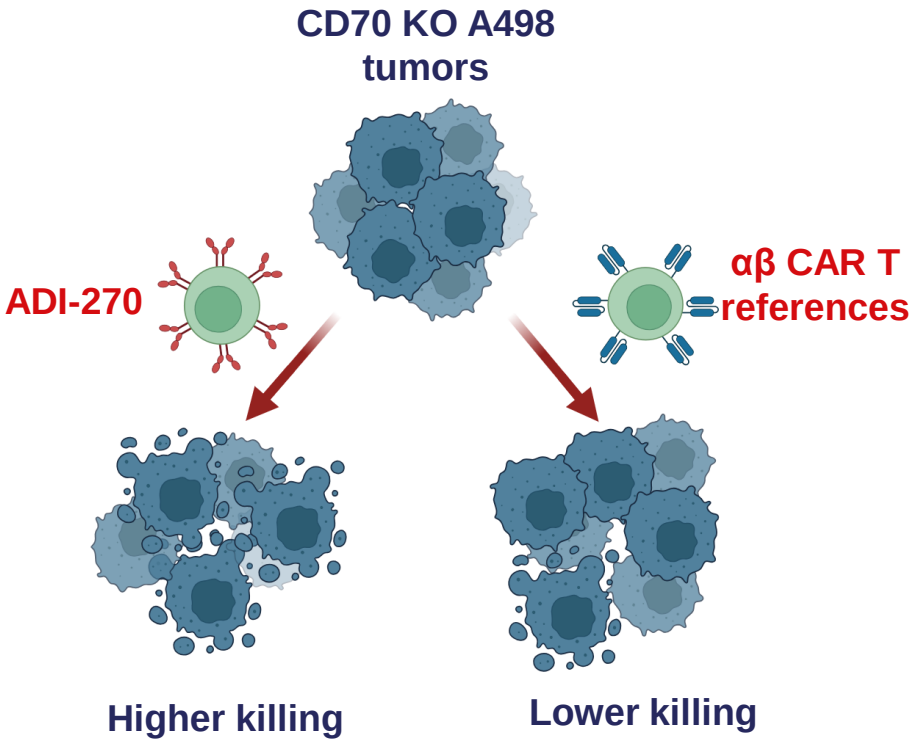


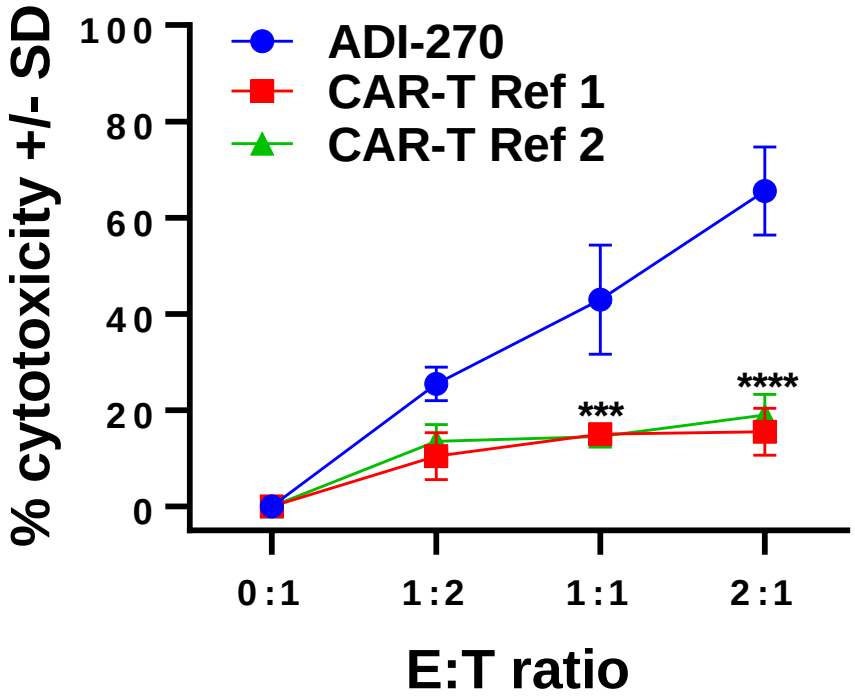


test materials derived from same donor PBMCs

E:T ratio = 1:1, N=2 donors, ****p<0.0001

ADI-270 demonstrated higher innate cytolytic activity against CD70 negative tumor cells compared to CAR-T cell references

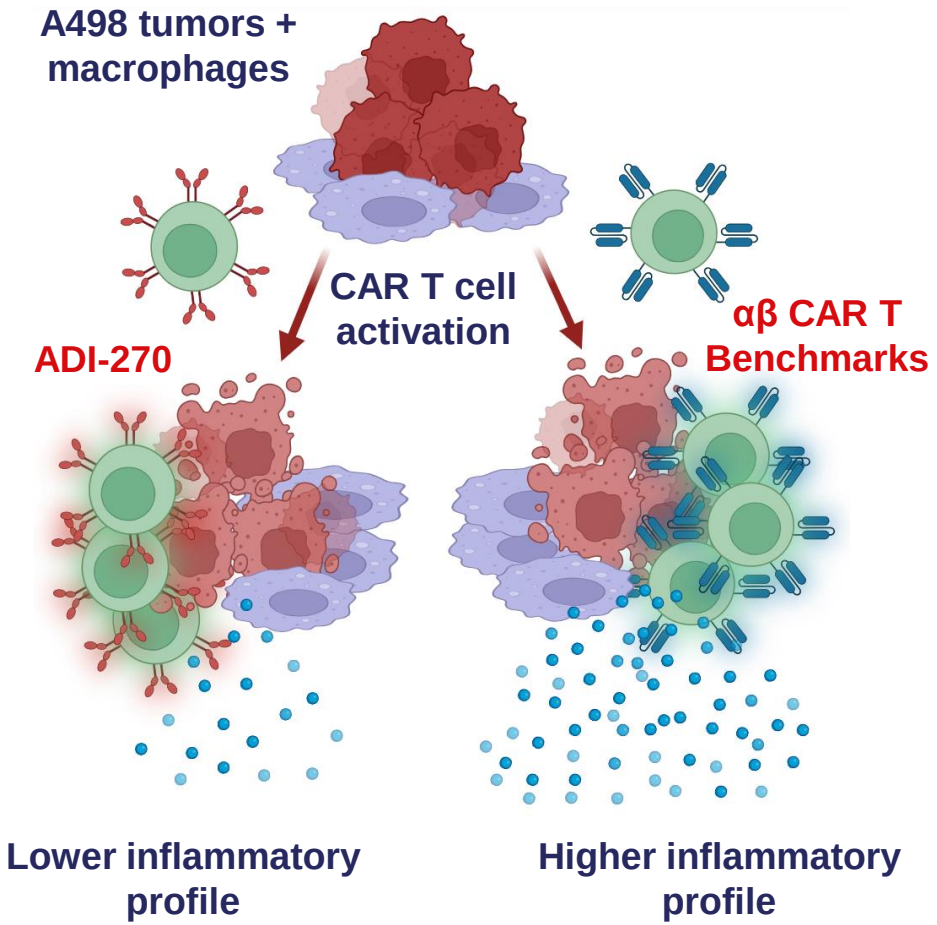


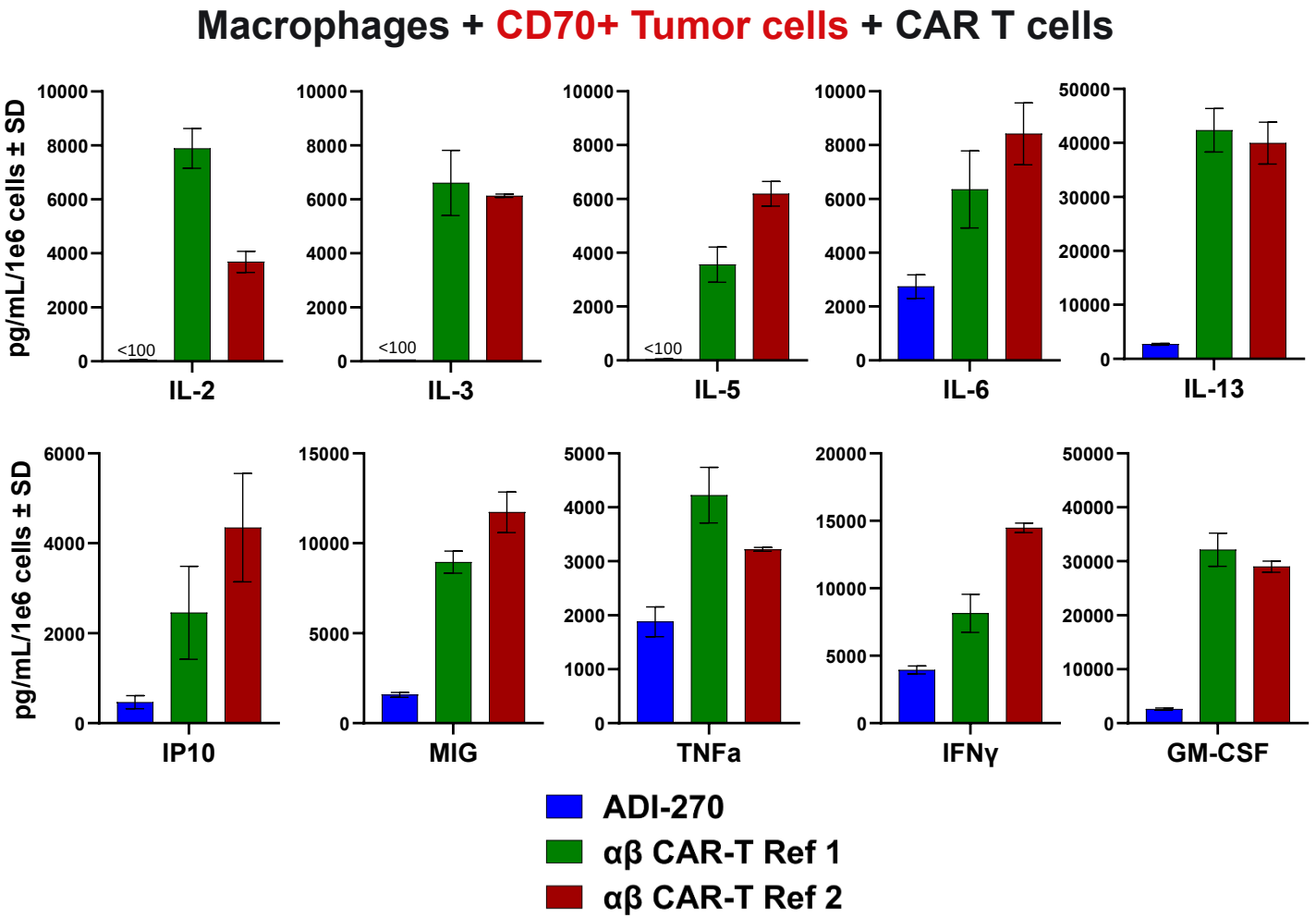


***p<0.001, ****p<0.0001

test materials derived from same donor PBMCs

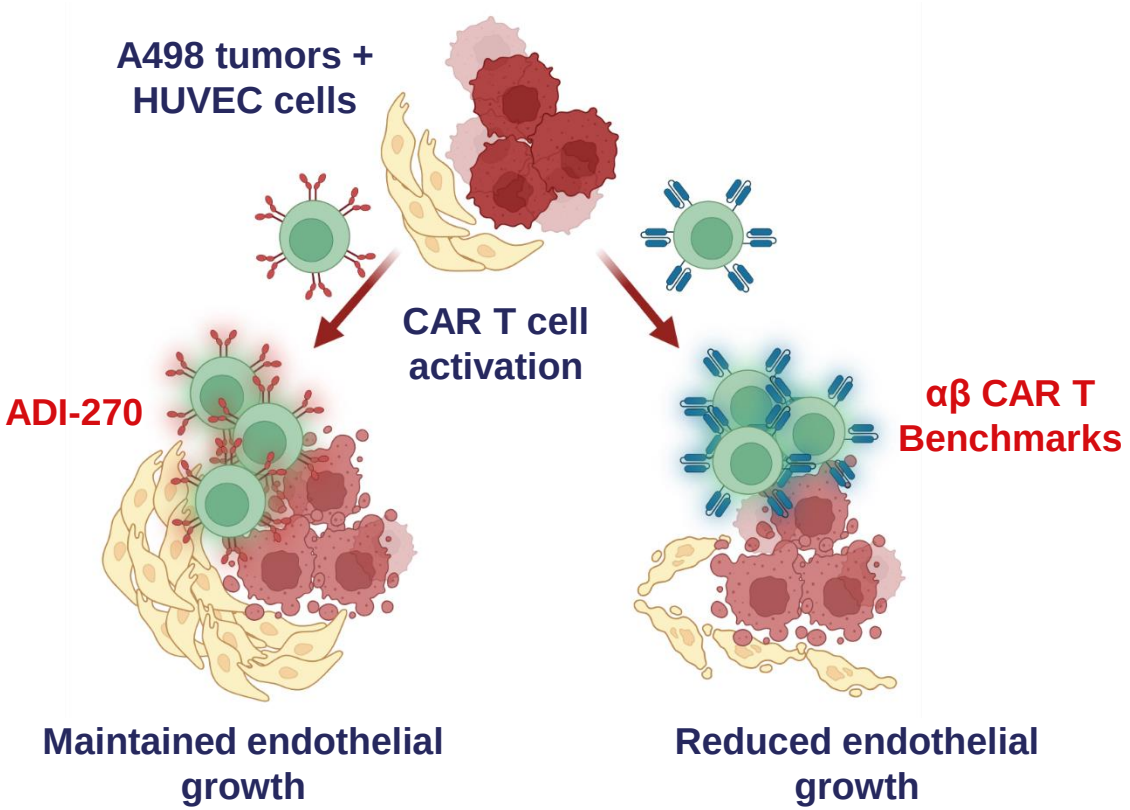
ADI-270 associated with a lower potential for macrophage activation syndrome and CRS compared to αβ CAR T cell benchmarks

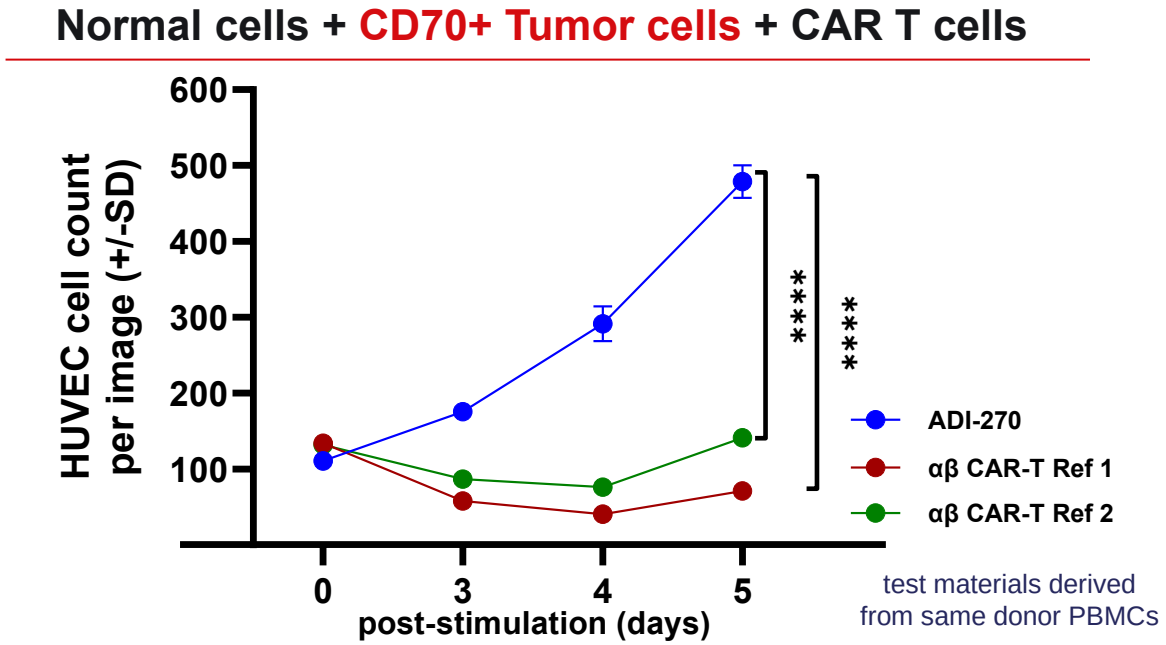


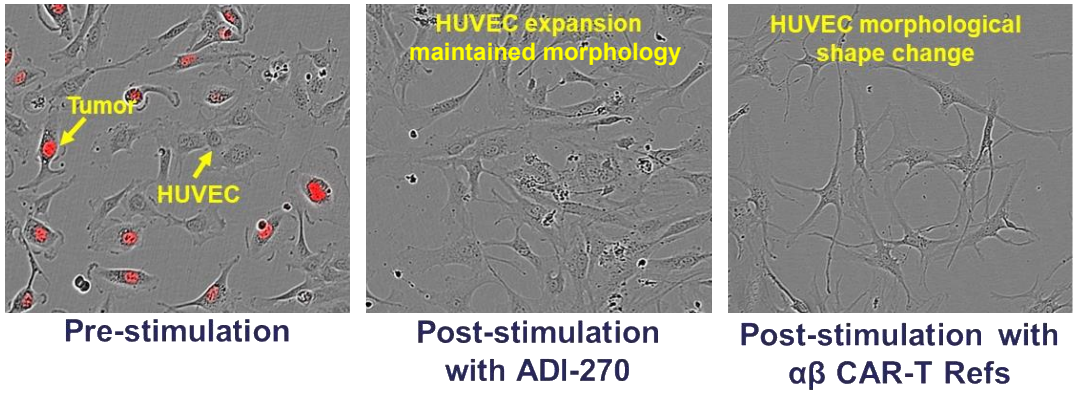


test materials derived from same donor PBMCs

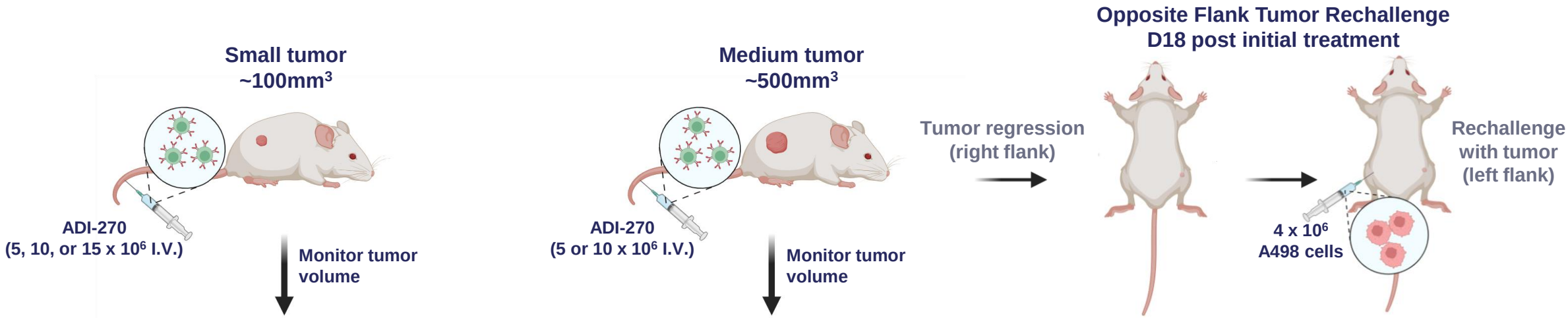
ADI-270 did not demonstrate activation-induced off-target toxicity compared to clinically relevant αβ CAR T cell benchmarks

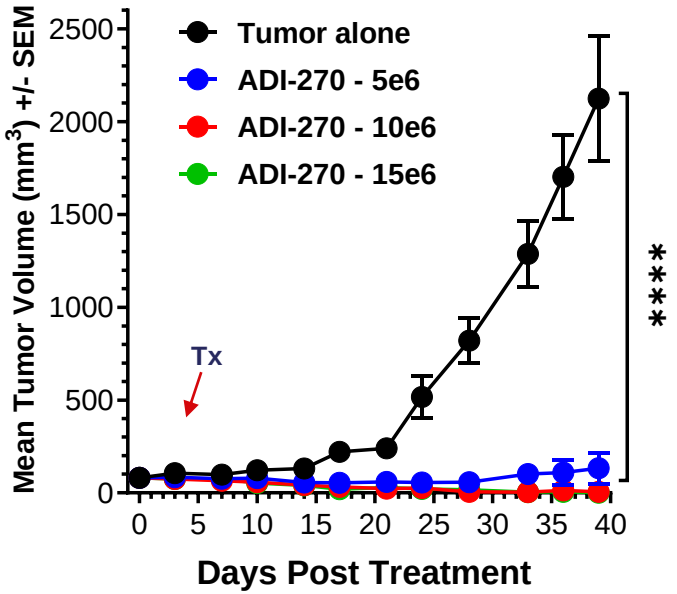


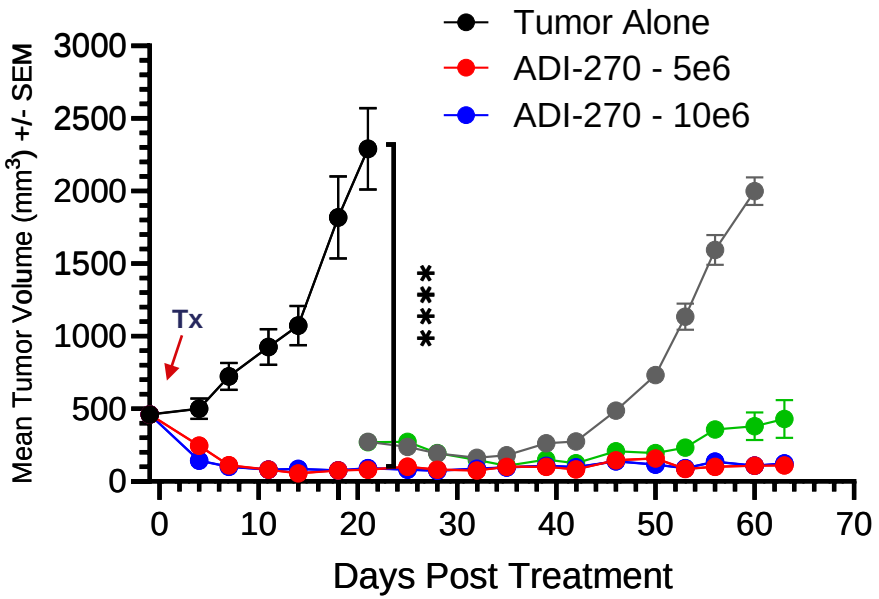


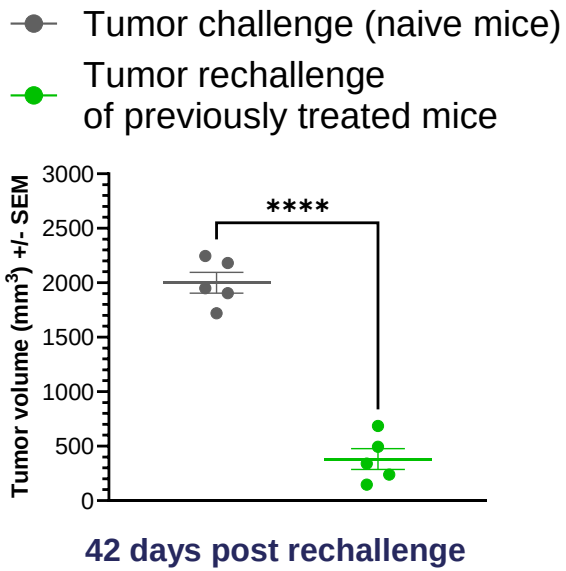


A single dose of ADI-270 showed potent regression and sustained systemic anti-tumor activity in ccRCC xenograft models





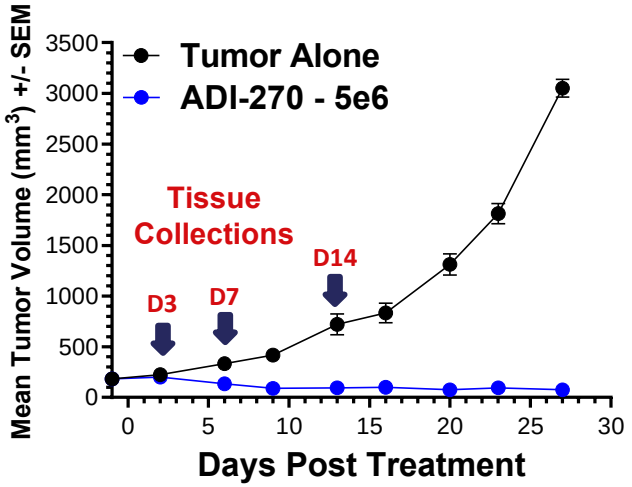


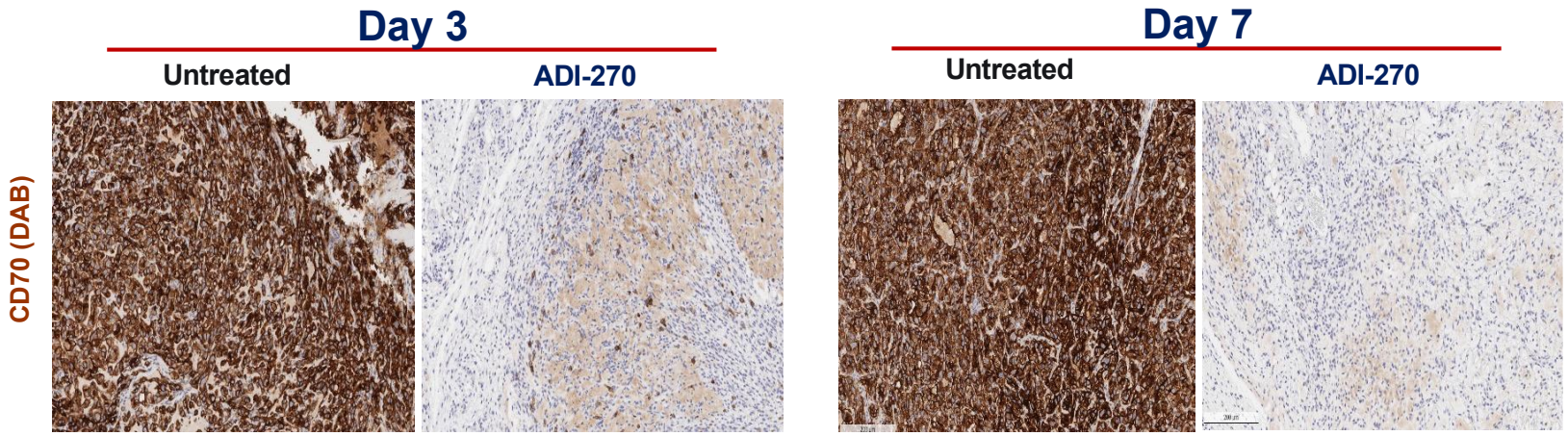


****p<0.0001

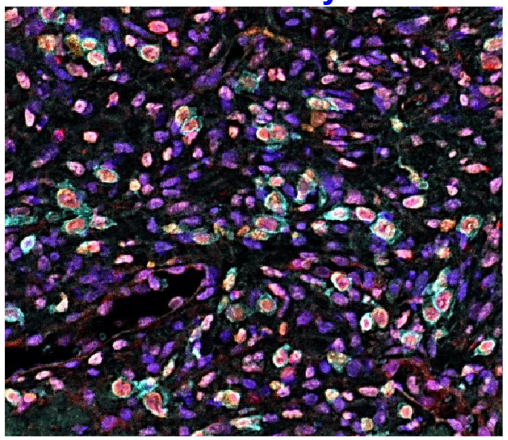
ADI-270 demonstrated rapid homing, activation and killing kinetics in ccRCC xenografts resulting in tumor and target eradication

A single dose of ADI-270 showed potent efficacy in A498 tumors, rapidly eradicating CD70+ cells



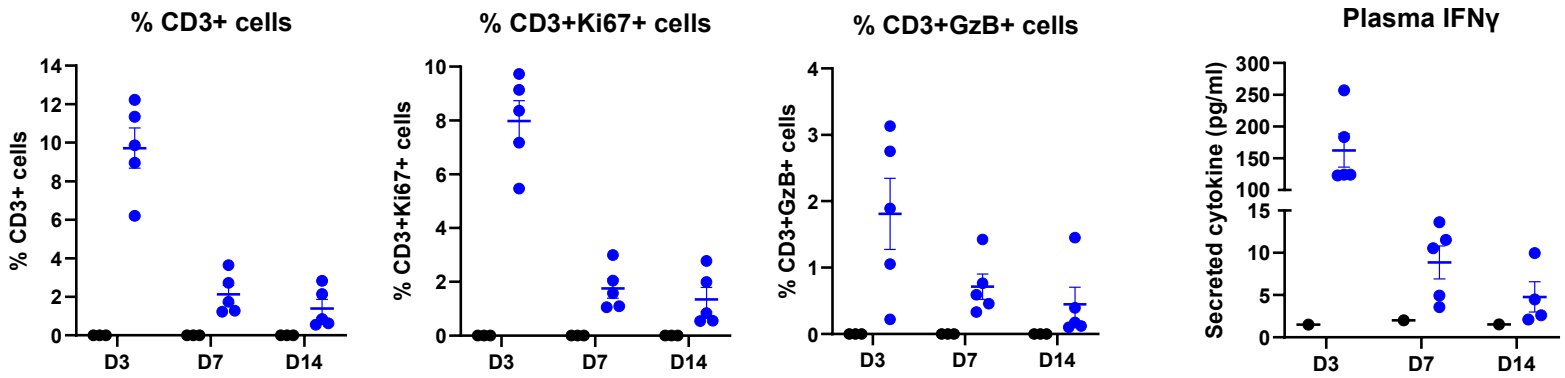


ADI-270 Day 3



DAPI +CD3 (cyan)+ Ki67 (orange) + Granzyme B (red)

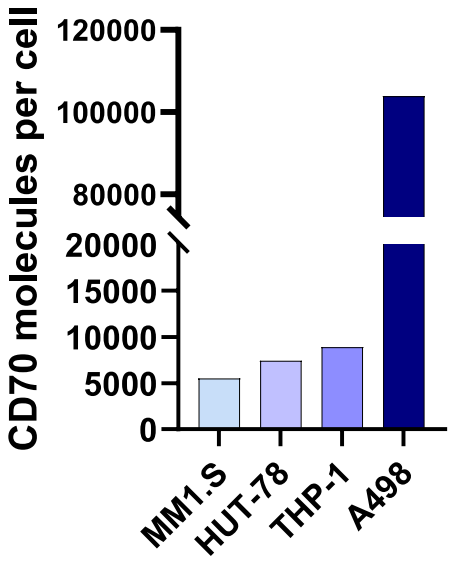
ADI-270 infiltrated and proliferated with effector function as early as Day 3



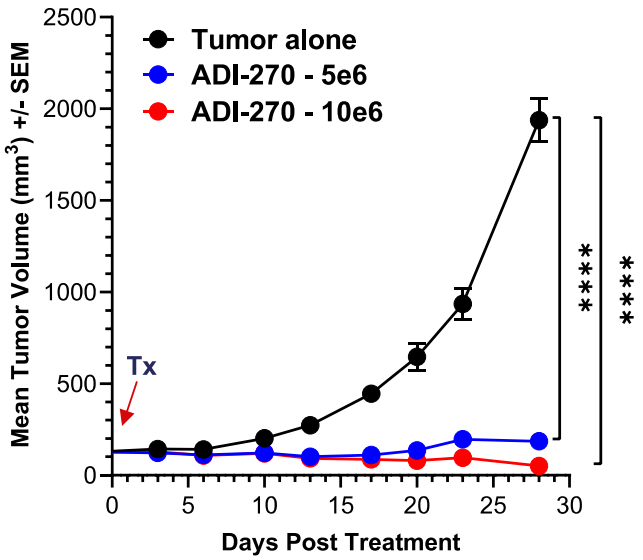
ADI-270 anti-tumor activity extended to multiple hematologic tumor xenografts associated with lower CD70 expression

A single dose of ADI-270 was administered IV into NSG mice harboring SC tumor xenografts

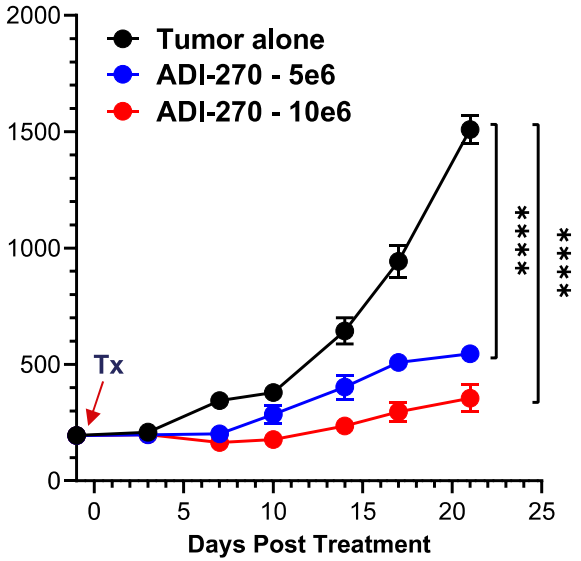
CD70 expression



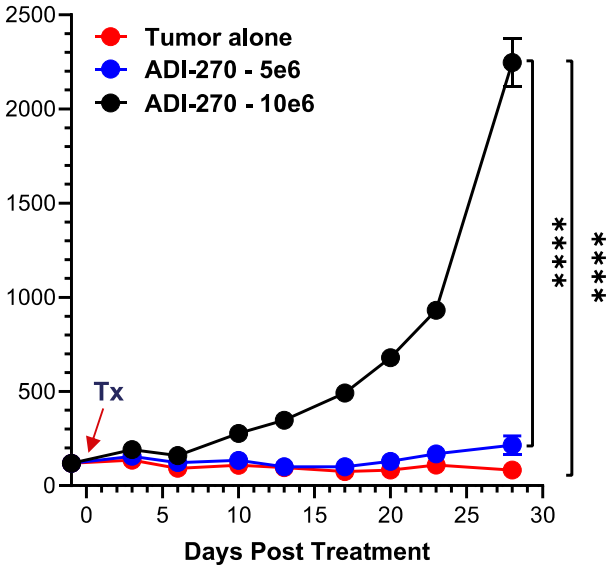
MM1.S (Multiple Myeloma)



HUT-78 (T Cell Lymphoma)



THP-1 (Acute Myeloid Leukemia)



Next steps: ADI-270

- ADI-270 represents potential evolution of γδ CAR T-cell based therapeutics
- CD27-based 3rd gen CAR demonstrated significant potency advantages[1,2,3,4]
- Armoring against TGFβ and alloreactive T cells confirmed and characterized preclinically
- Robust efficacy maintained across multiple relevant tumor models of varying stringency
- Desirable preclinical safety profile with lower potential for CRS and macrophage activation syndrome
- IND submission in ccRCC expected Q2 2024

[1]Shaffer et al., Blood 2011
[2]Acharya et al., Blood 2023
[3]Leick et al., Cancer Cell 2022
[4]Kasap et al., BioRxiv 2024

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