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ADI-270, an armored allogeneic anti-CD70 CAR γδ T cell therapy, demonstrates robust CAR-directed and -independent anti-tumor activity against hematological and solid tumor models compared to conventional CAR αβ T cells

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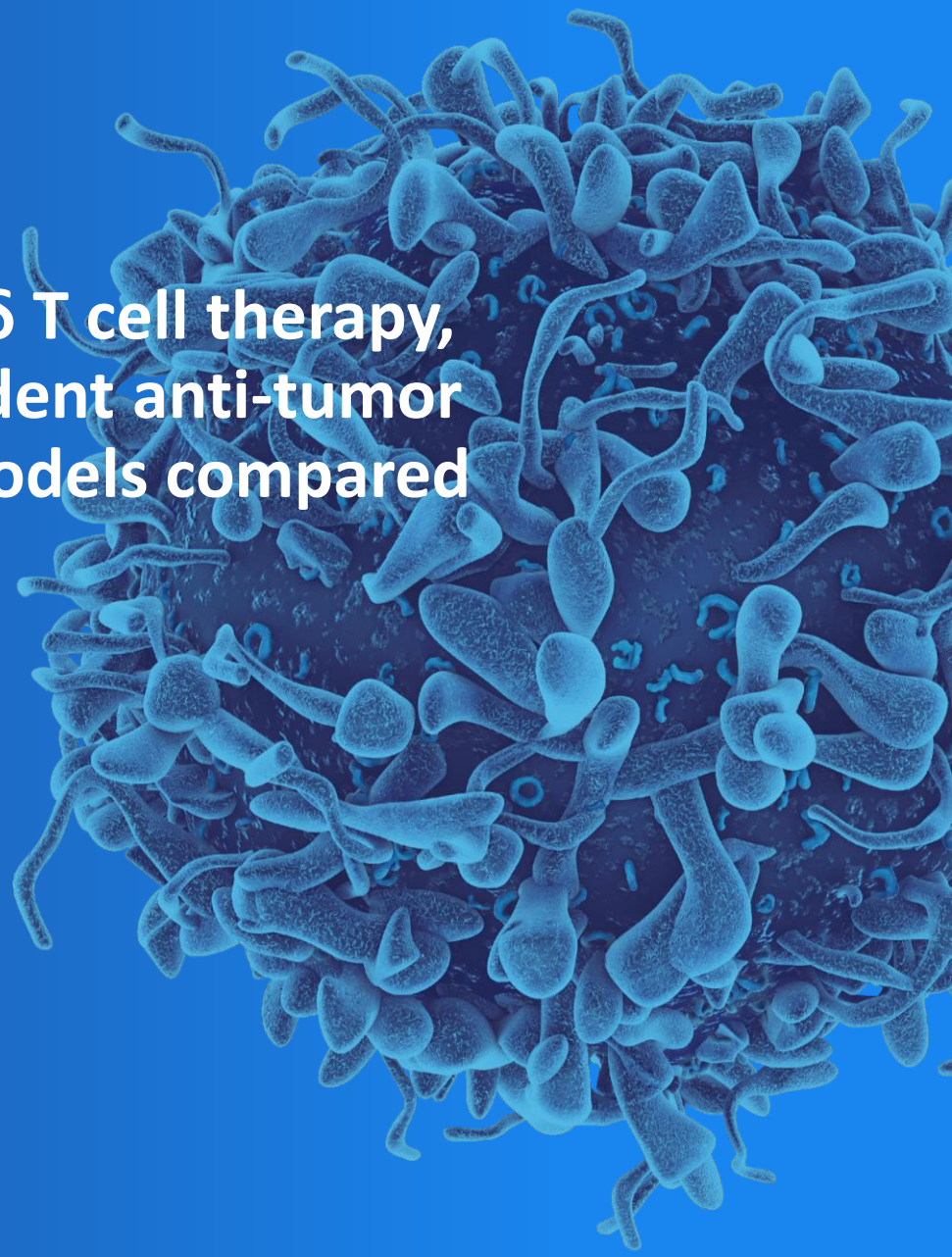
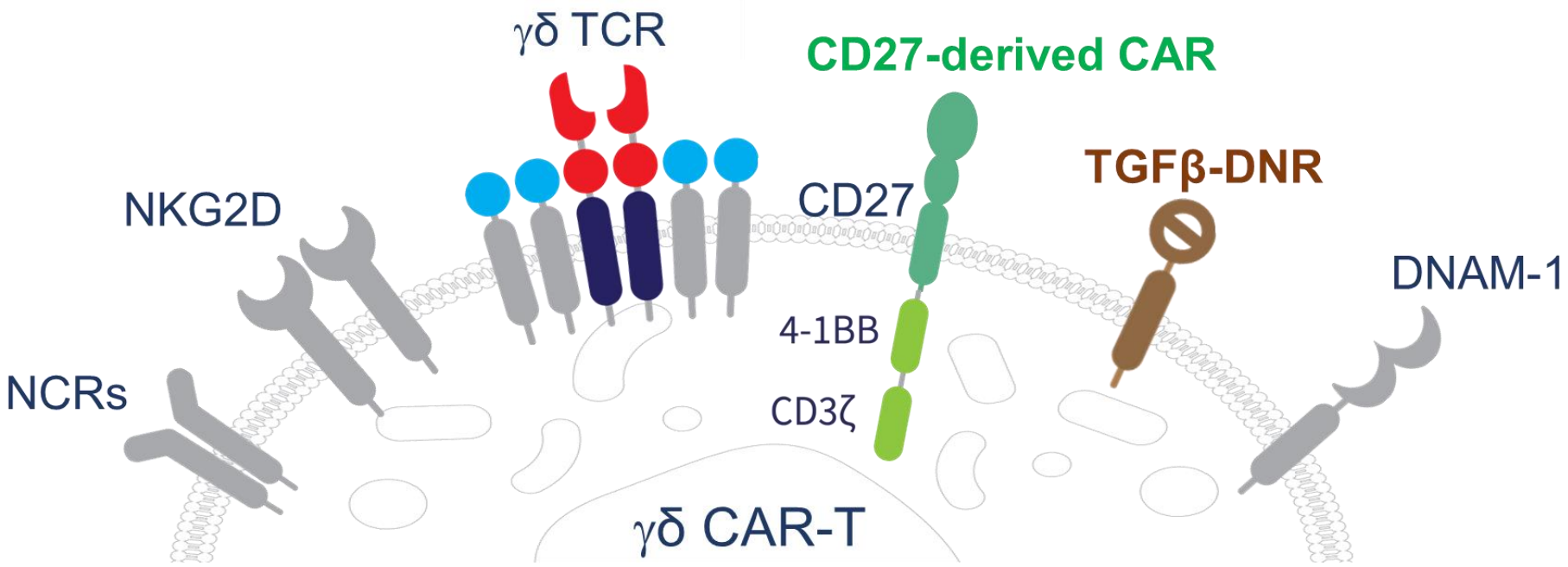
28th ASGCT Annual Meeting 2025
New Orleans, LA



Disclosures: Melinda Au

An employee and shareholder of Adicet Bio

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 $CD70^+$ T cells to increase persistence
- Combines endogenous γδ innate and adaptive mechanisms to recognize and kill malignant cells

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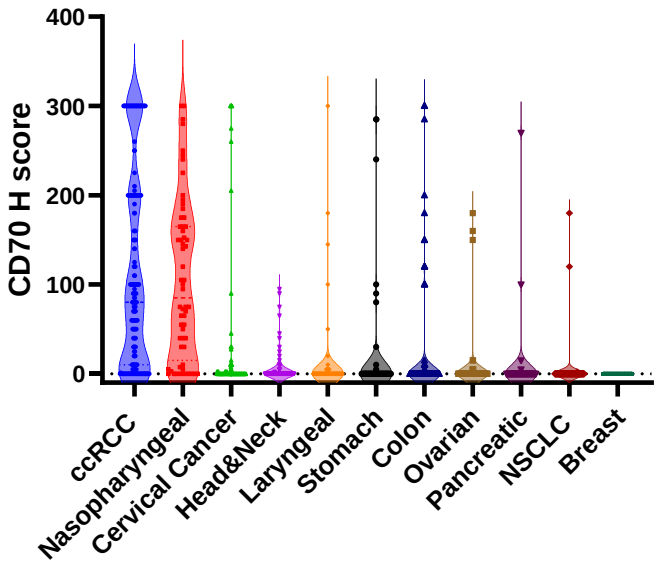
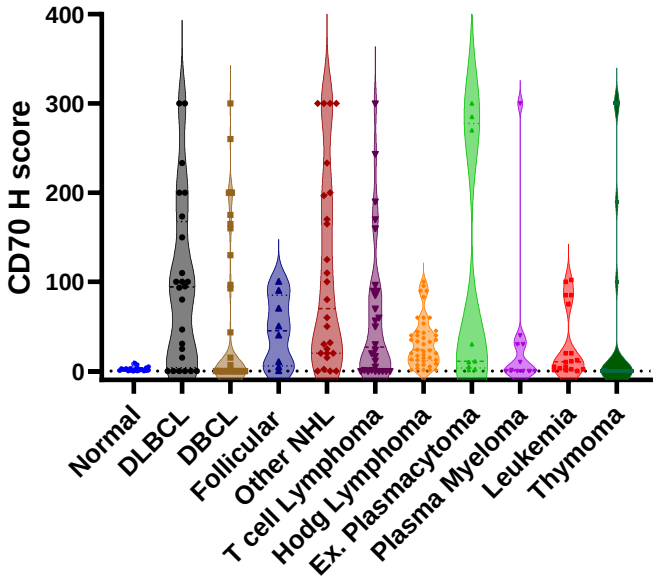
CD70 is expressed on multiple solid and hematological cancers with limited expression in normal tissues

- 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 (immune cells)
- Clinically established safety profile

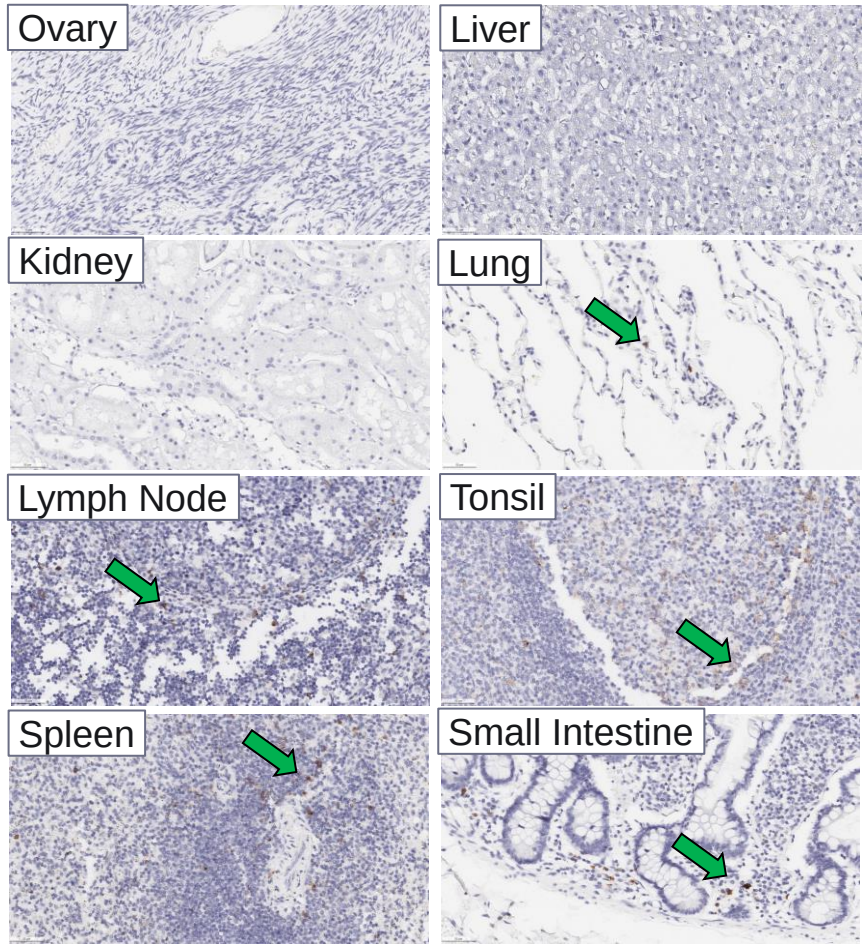
Solid tumors



Hematological malignancies



Representative images from a normal tissue array stained for CD70



Adicet Bio internal data; unpublished

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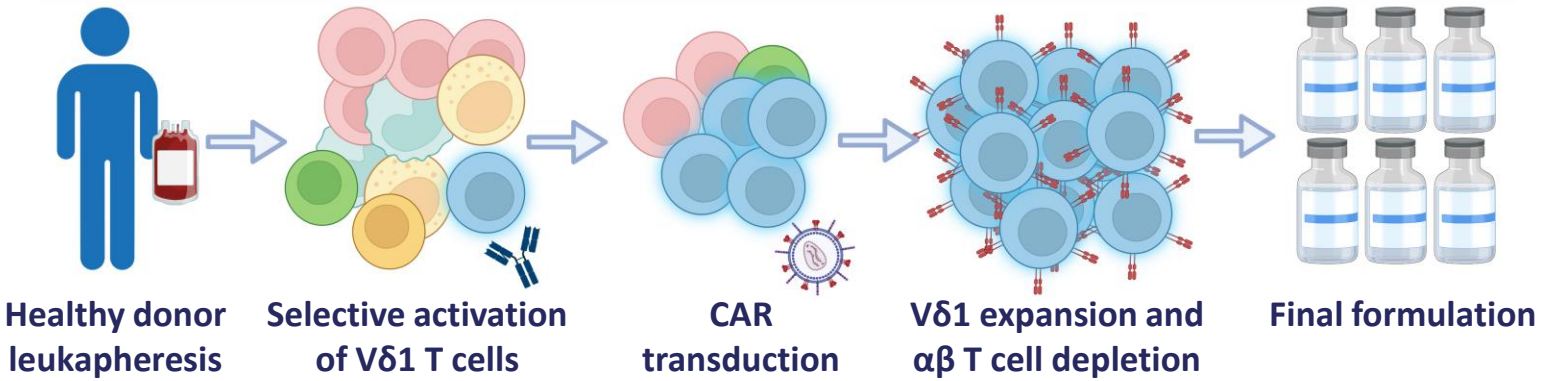
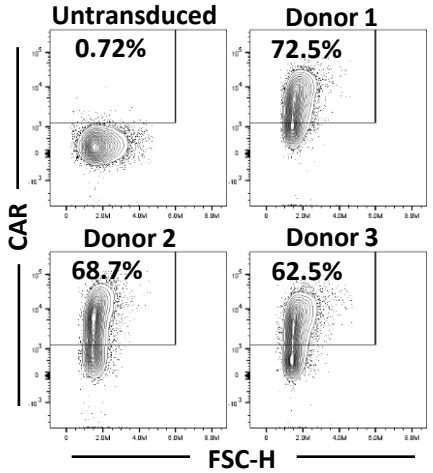
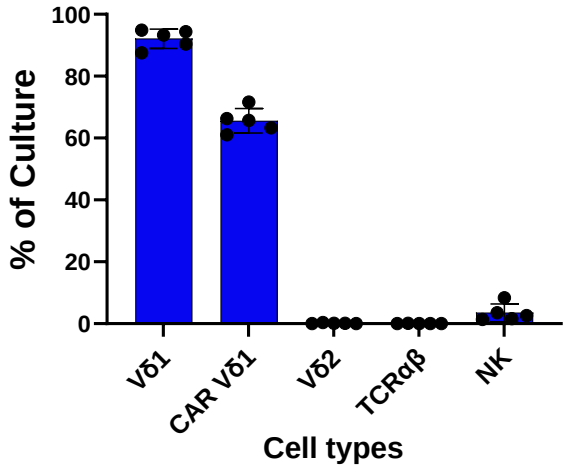
ADI-270 product highly enriched for Vδ1 and memory phenotype

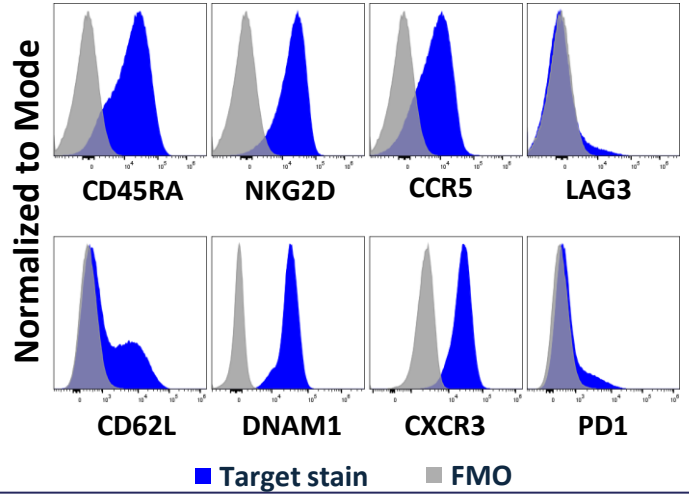


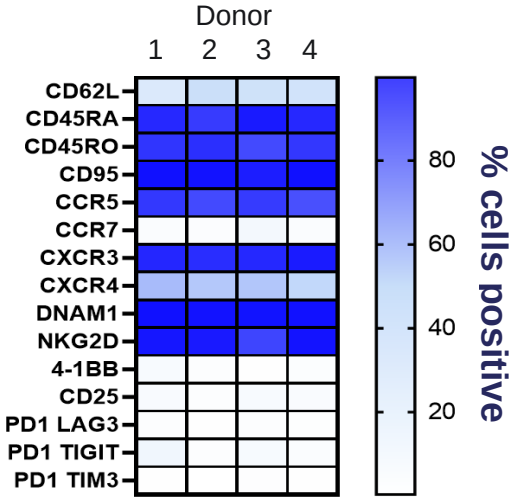


ADI-270 final product is highly pure for Vδ1 T cells



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





Adicet Bio internal data; unpublished

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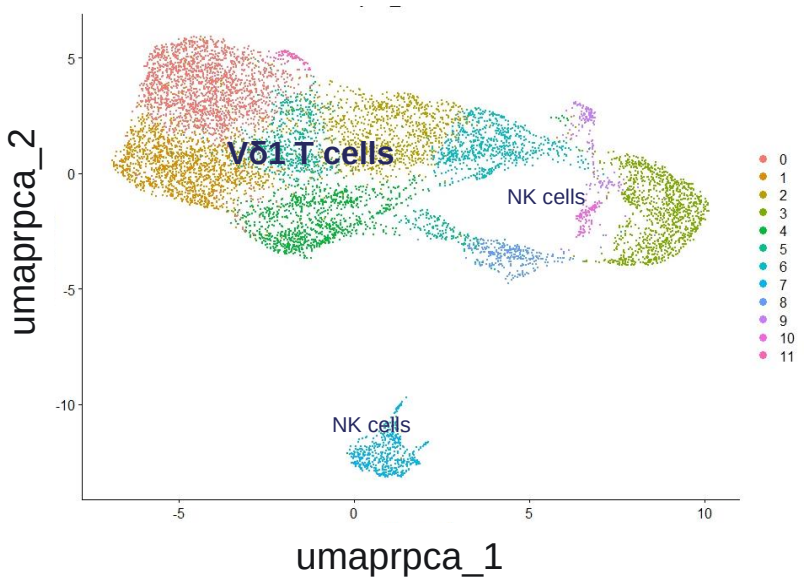
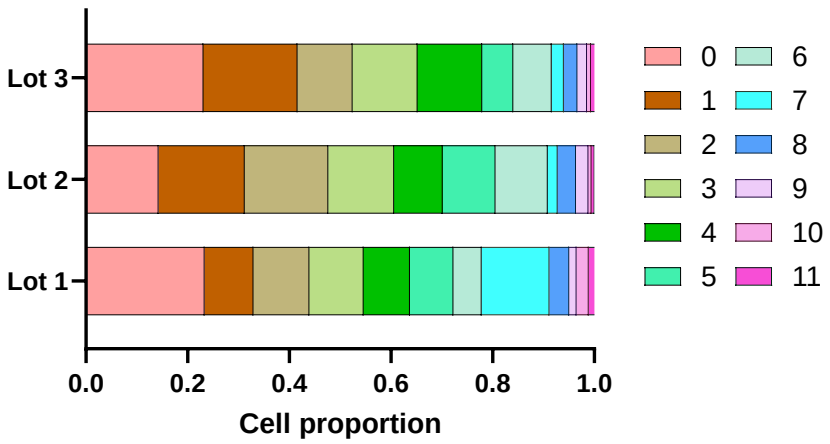
High degree of similarity between cells within ADI-270 lots from scRNA sequencing profiles

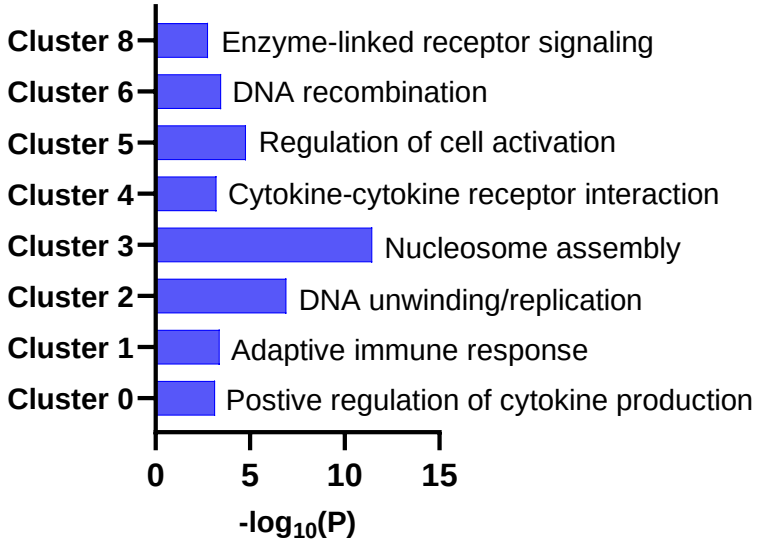
Majority of UMAP clusters are spatially grouped together



Cell proportions across clusters are similar in ADI-270 lots



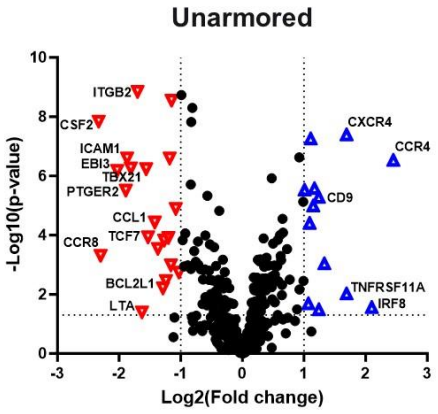
Pathways associated with clusters in Vδ1 T cells from ADI-270 lots



NK cell clusters and those without a defined pathway were excluded.

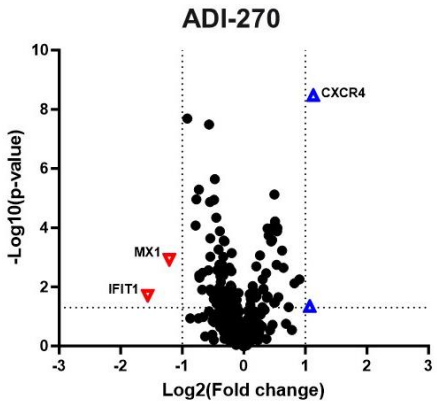
ADI-270 is resilient to the inhibitory effects of TGFβ

ADI-270 is resilient to transcriptional changes driven by TGFβ signaling



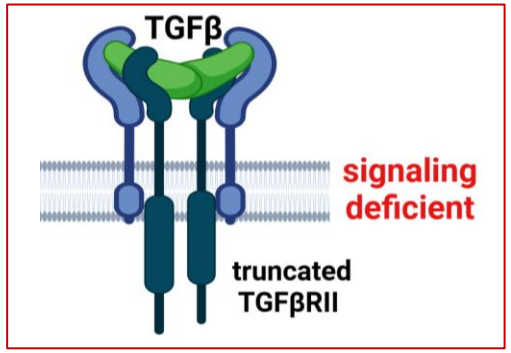
Genes upregulated in presence of TGFβ

Genes downregulated in presence of TGFβ

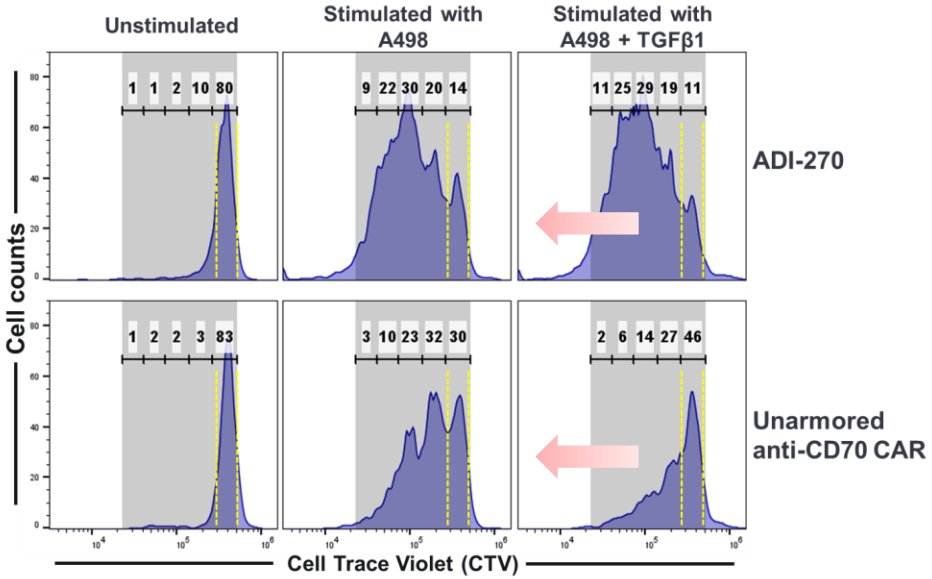


Genes upregulated in presence of TGFβ

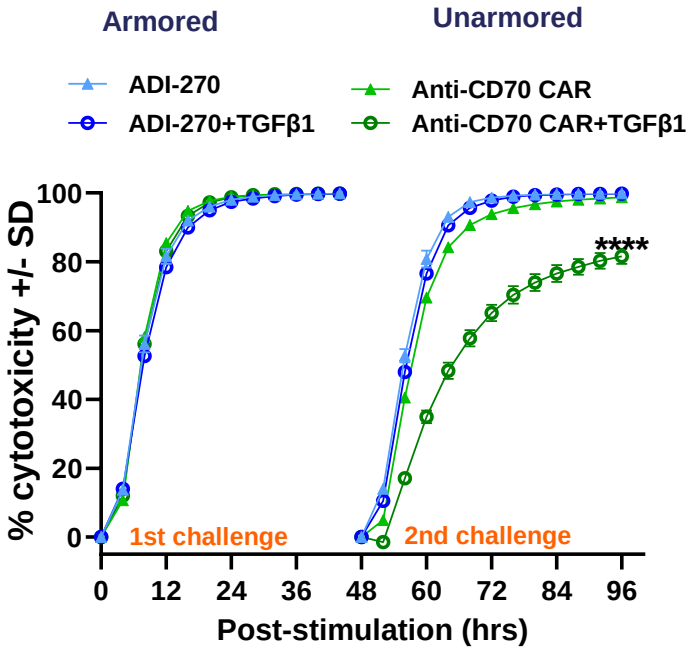
Genes downregulated in presence of TGFβ



ADI-270 maintains proliferation in the presence of TGFβ1

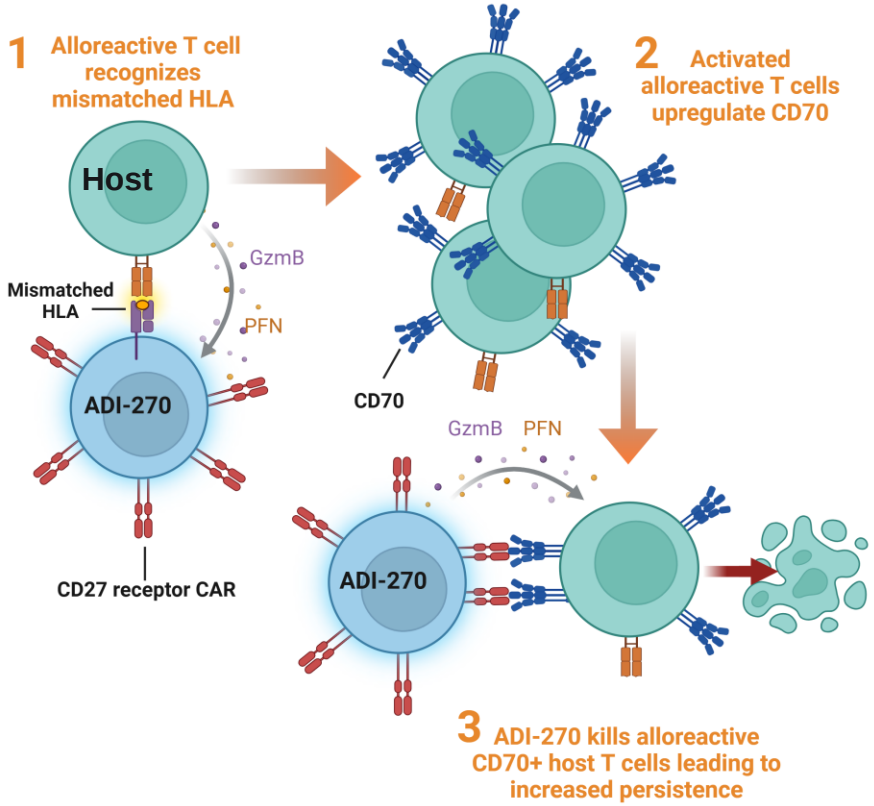


ADI-270 maintains cytotoxicity in the presence of TGFβ1

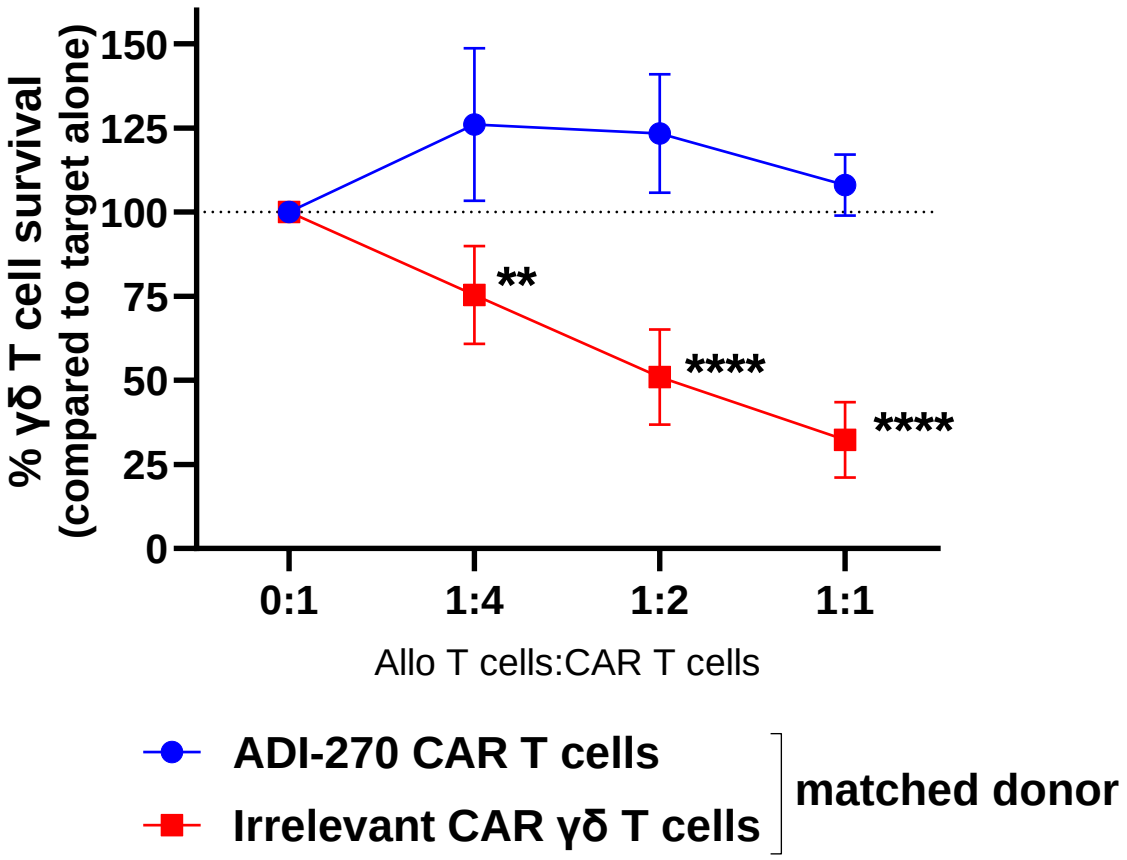


CD70-targeting armors ADI-270 against alloreactive host T cells

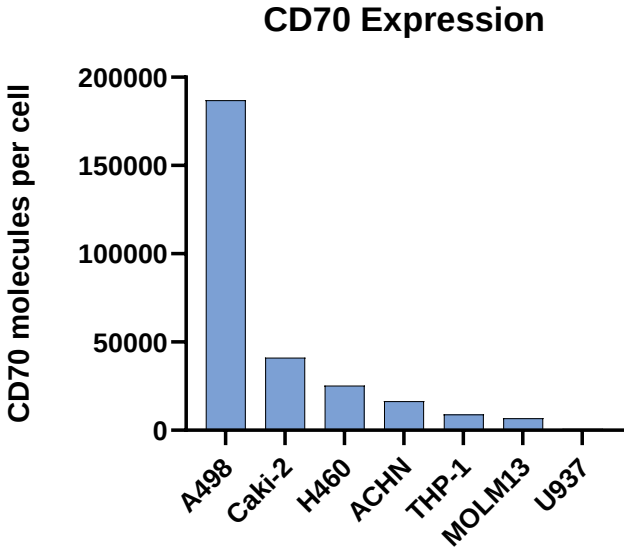
Proposed MoA for enhanced persistence of ADI-270

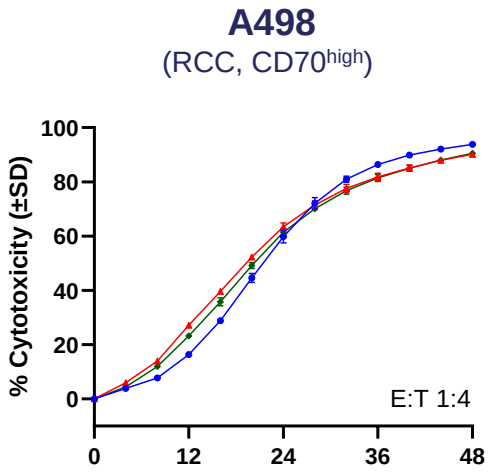


ADI-270 persists in culture with primed alloreactive T cells derived from 3 donors

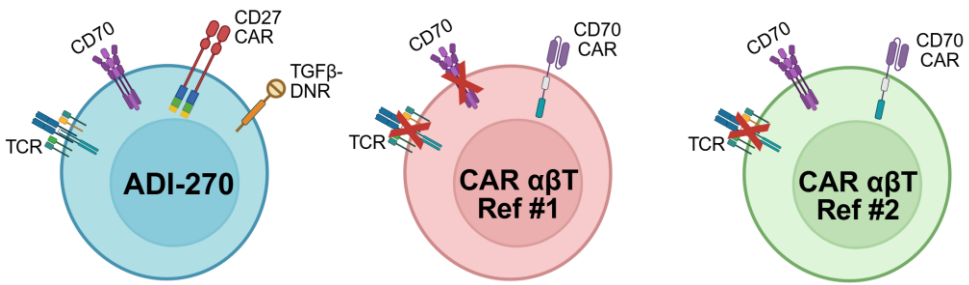


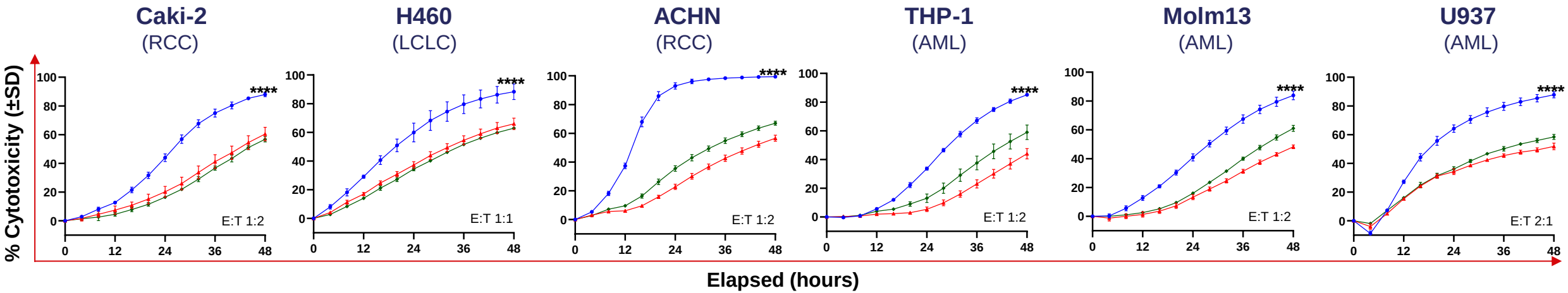
ADI-270 demonstrates greater cytotoxicity compared to CAR αβ T cell references against CD70^{low} tumor cell lines





Allogeneic αβ T cells were engineered to express clinically tested scFv-based anti-CD70 CARs





ADI-270 — CD70 CAR αβT Ref #1 — CD70 CAR αβT Ref #2

****p < 0.0001 (ADI-270 vs CAR αβ T references)

Adicet Bio internal data; unpublished

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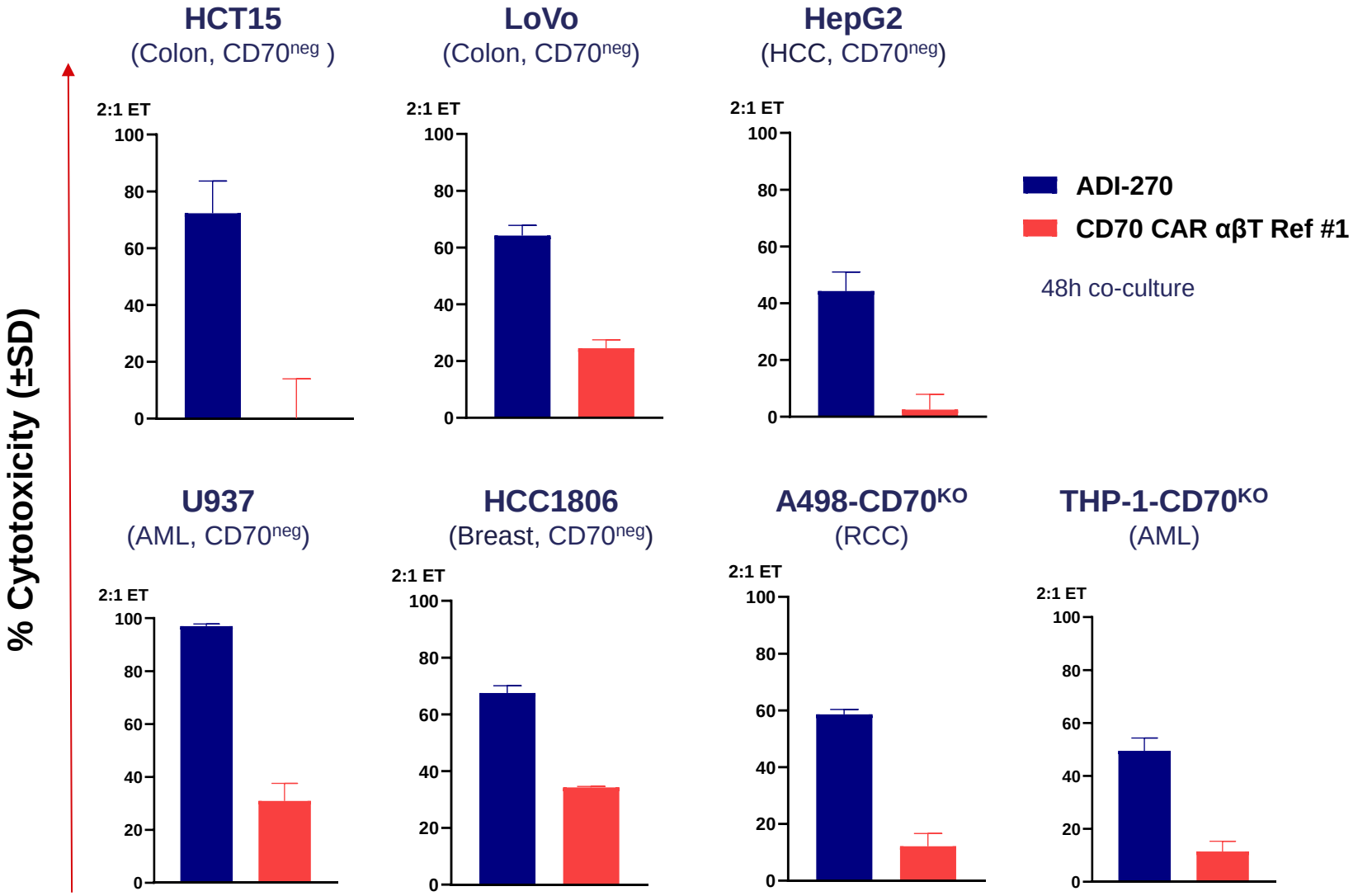
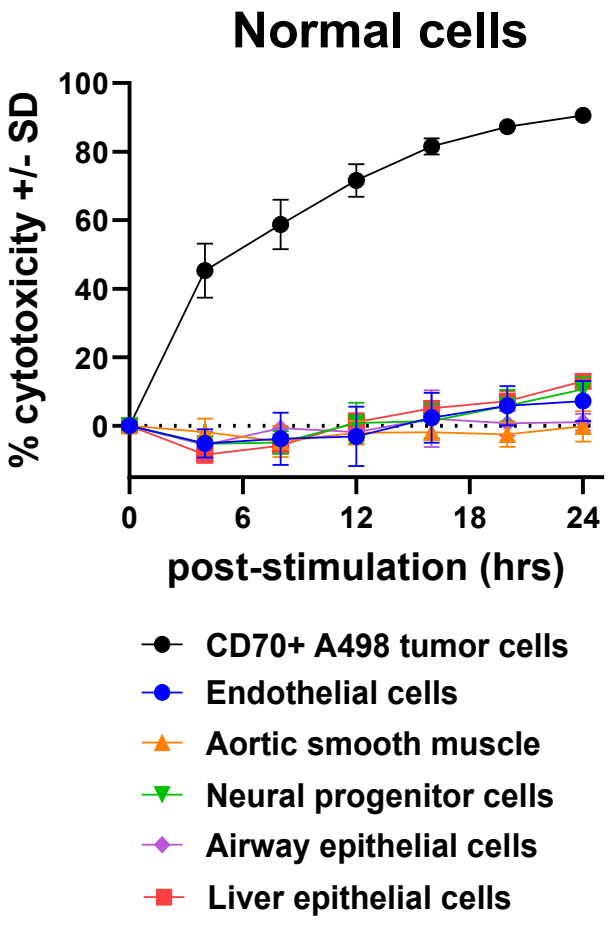
ADI-270 exhibits increased innate activity against CD70-negative tumor cell lines compared to a CAR αβ T cell reference



ADI-270 has no cytotoxicity against normal primary CD70neg cells



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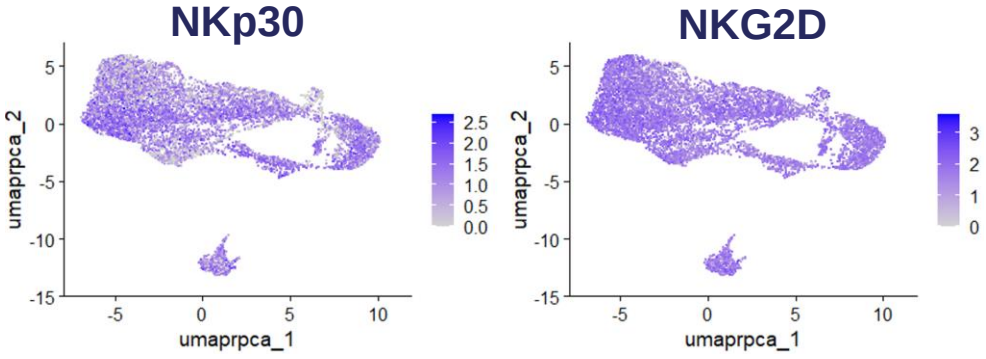
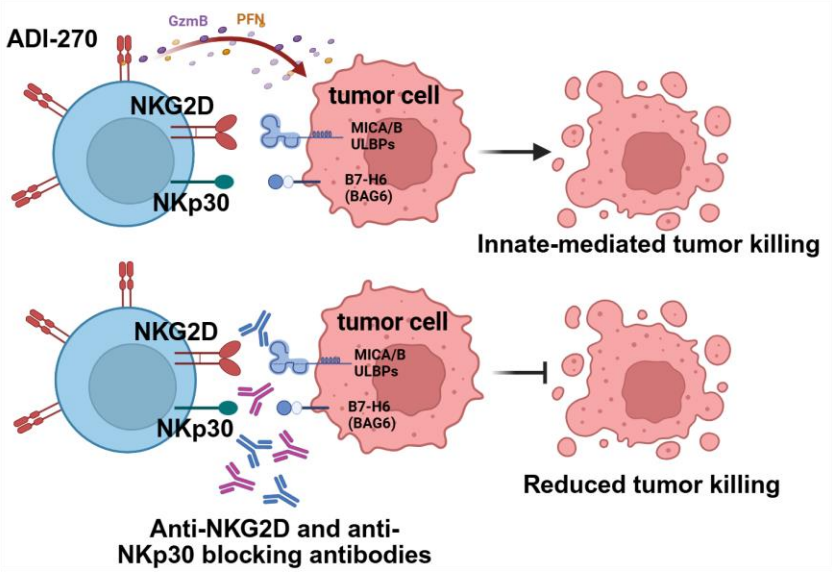
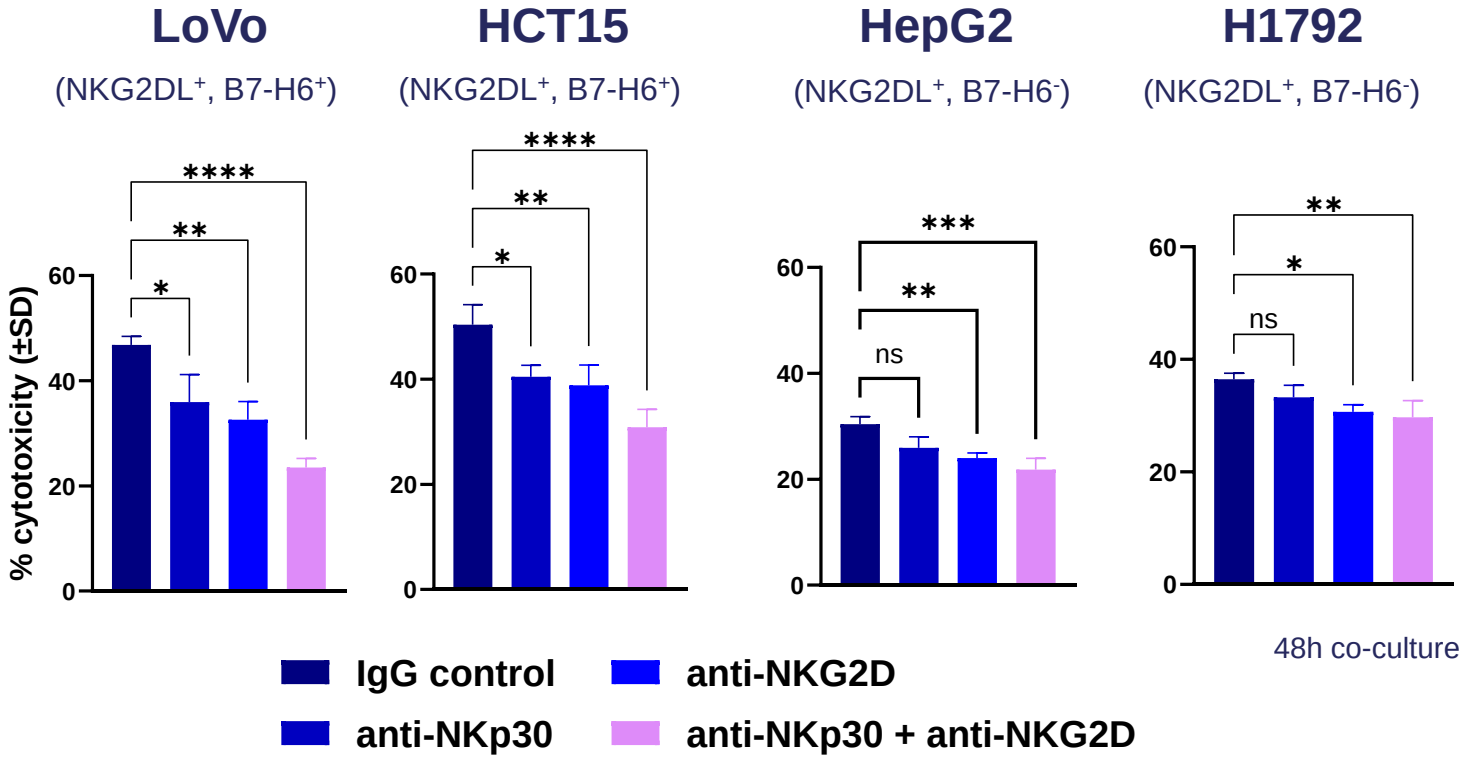
NKp30 and NKG2D on ADI-270 synergistically mediated innate immunity against CD70^{neg} tumor cell lines

ADI-270



Antibody Blocking Study



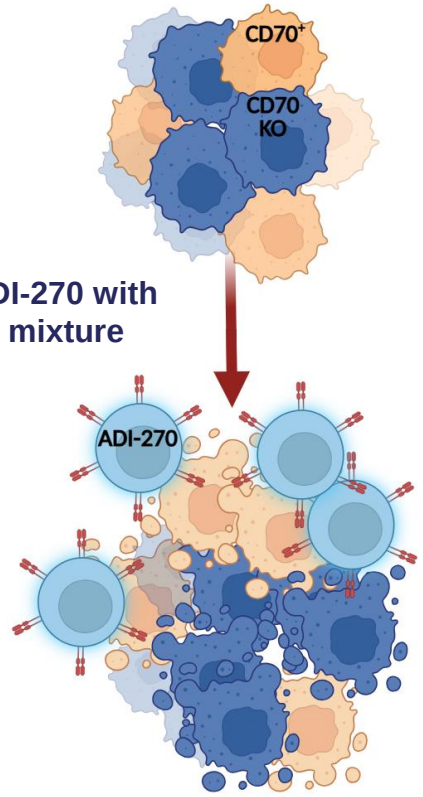


48h co-culture

NKG2DL$^+$, B7-H6$^+$ tumor cell lines (LoVo and HCT15) induced greater synergistic reduction of cytotoxicity through NKp30 and NKG2D blocking than NKG2DL$^+$, B7-H6$^-$ tumor cell lines (HepG2 and H1792)

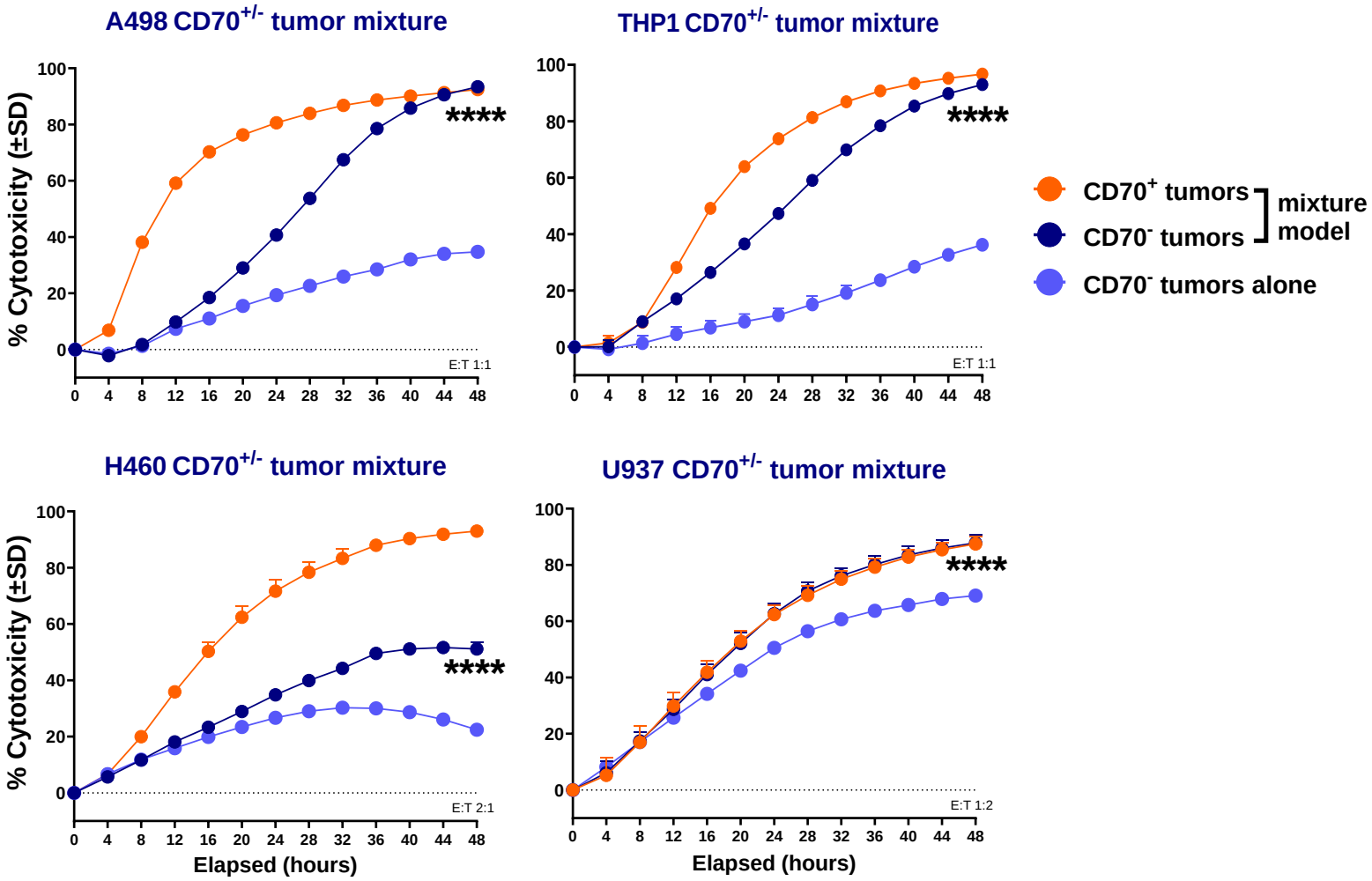
ADI-270 is associated with both CAR-dependent and innate mechanisms for targeting tumors

CD70$^{+/-}$ tumor mixture model



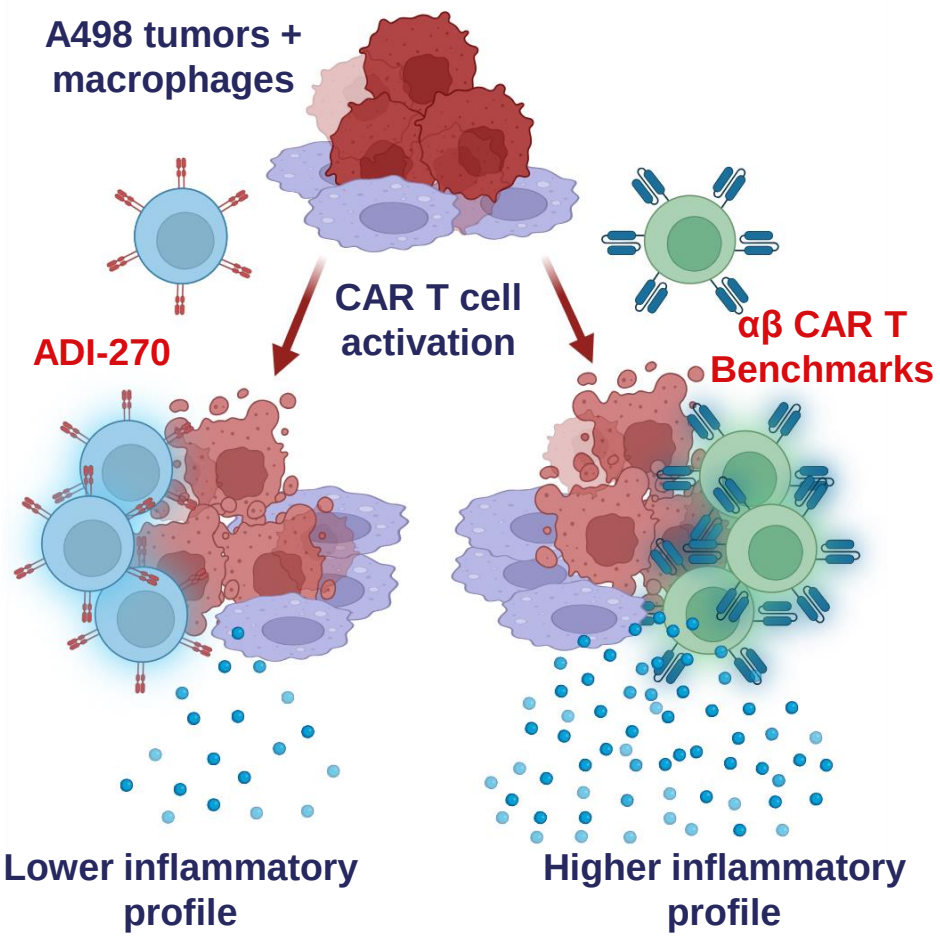
Co-culture of ADI-270 with CD70$^{+/-}$ tumor mixture

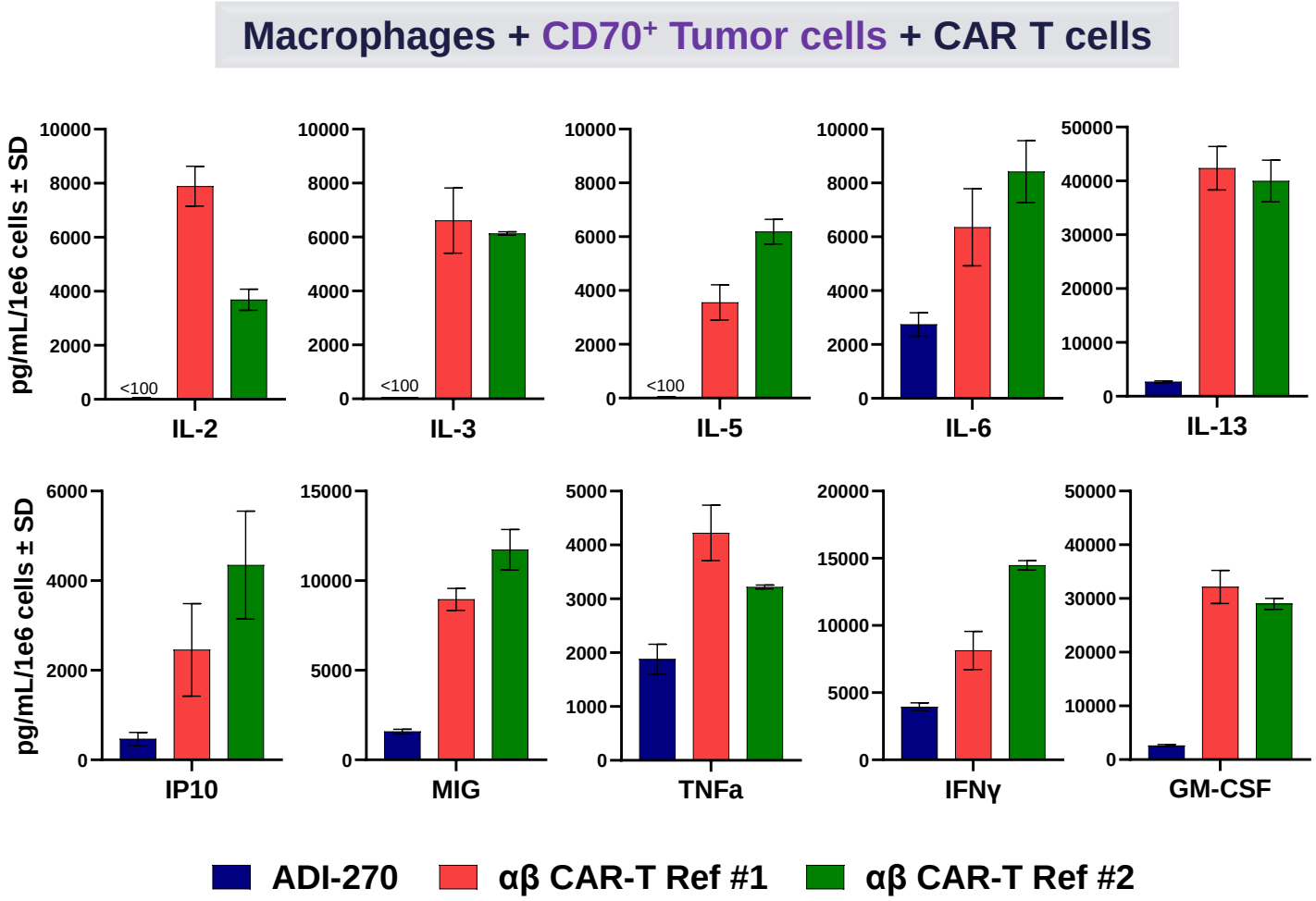
Increased killing of CD70^{-} tumors within the tumor mixture



****p<0.0001 (CD70^{-} tumors killed in mixture model vs CD70^{-} alone)

ADI-270 is 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

Adicet Bio internal data; unpublished

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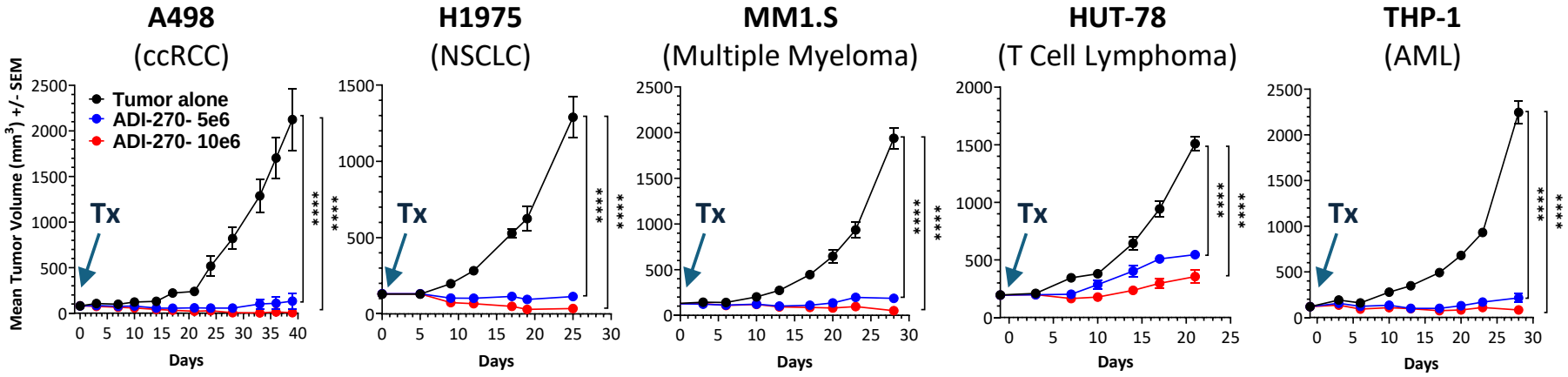
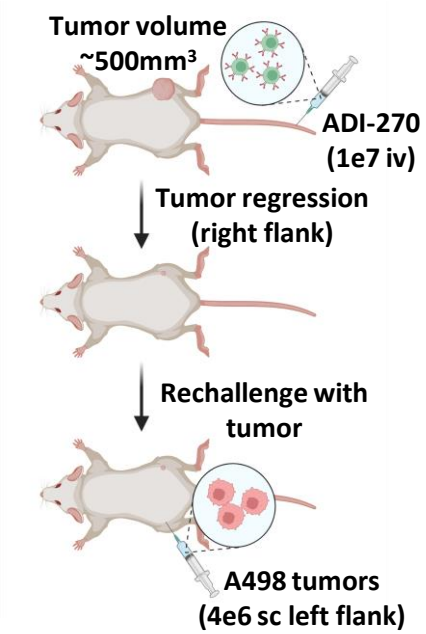
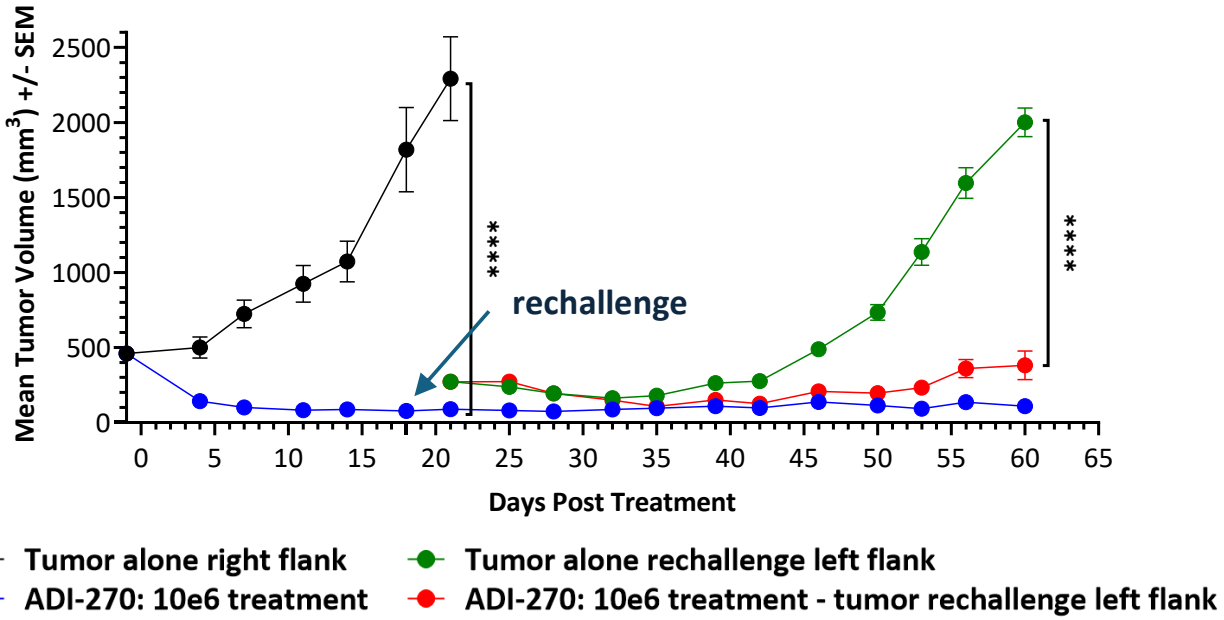
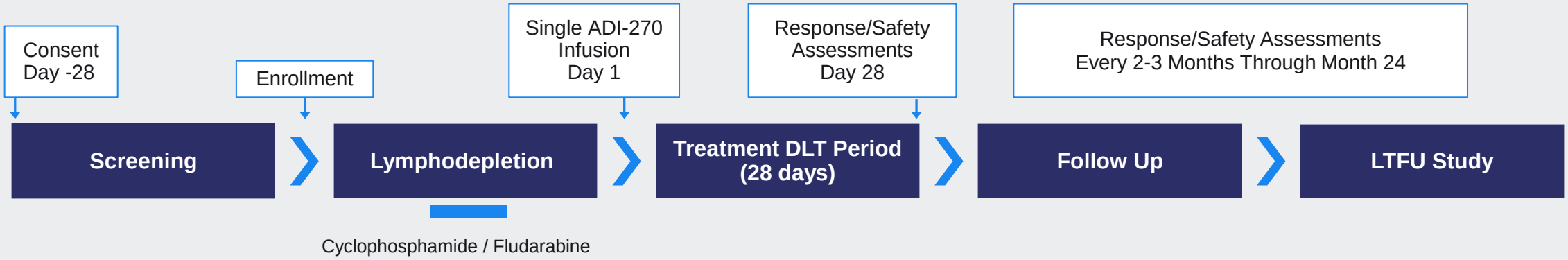
ADI-270 anti-tumor activity extends to multiple solid and hematologic tumor xenografts



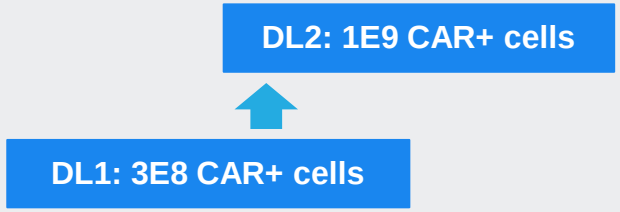




ADI-270 Phase I Study



Dosing Arms:



3+3 design

Primary endpoints:

- Number of DLTs
- Treatment emergent and treatment-related AEs

Secondary endpoints:

- ORR, DOR, PFS, TTP, and OS
- PK, host immune cell recovery

Dose Expansion:

- ccRCC
- Other CD70^{+} tumors

Clinical protocol enables to de-escalate down to DL-1 of 1E8 CAR+ Cells; Patients meeting CR, PR or SD per RECIST v1.1 may be eligible to a second dose of ADI-270 following within the first 6 month from initial dose

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Acknowledgments

Adicet's Mission
Deliver Best-in-Class Gamma Delta Therapies for Patients Fighting Autoimmune Disorders and Cancer

Adicet Bio