Fate THERAPEUTICS

Better Cells For Better Therapies™

Programmed Cellular Immunotherapies

iPSC-derived, Off-the-Shelf Cancer Immunotherapies

November 30, 2018

Forward-Looking Statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the Company's advancement of and plans related to the Company's product candidates and clinical studies, the therapeutic potential of the Company's iPSC-derived cell products, including FT500, FT516, FT596 and FT819, the Company's regulatory strategy and advancement of its clinical studies, and the Company's plans for its intended clinical investigation of its iPSC-derived cell products, including FT500. These and any other forward-looking statements in this presentation are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk of cessation or delay of ongoing or planned development and clinical activities for a variety of reasons (including requirements that may be imposed by regulatory authorities on the initiation or conduct of clinical trials or to support regulatory approval, or on the manufacture of its product candidates, any adverse events or other results that may be observed during development, or difficulties in manufacturing or supplying the Company's product candidates for clinical trials), the risk that results observed in preclinical studies of its iPSC-derived cell products, including FT500, may not be replicated in ongoing studies or future clinical trials, and the risk that its iPSC-derived cell products, including FT500, may not produce therapeutic benefits or may cause other unanticipated adverse effects. These statements are also subject to other risks and uncertainties as further detailed in the Company's most recently filed periodic report, and subsequent periodic reports filed by the Company, under the Securities Exchange Act of 1934, as amended, any of which could cause actual results to differ materially from those contained in or implied by the forward-looking statements in this presentation. The Company is providing the information in this presentation as of the date hereof and does not undertake any obligation to update any forward-looking statements contained in this presentation unless required by applicable law.

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iPSC-derived, Off-the-Shelf Cancer Immunotherapies

Agenda

- Welcome – *Scott Wolchko, President & CEO*
- iPSC Platform & Pipeline Overview – *Bob Valamehr, PhD, CDO*
- FT500 + CPB: Bridging Innate and Adaptive Immunity – *Jeff Miller, MD*
- Enhancing CD16 and CAR Biology for NK cells – *Dan Kaufman, MD PhD*
- iPSC-derived Cell Product Pipeline – *Bob Valamehr, PhD, CDO*
- Creating an Off-the-Shelf CART Platform – *Michel Sadelain, MD PhD*
- Concluding Remarks – *Scott Wolchko, President & CEO*

Fate Therapeutics Announces FDA Clearance of Landmark IND for FT500 iPSC-derived, Off-the-Shelf NK Cell Cancer Immunotherapy

Company to Initiate First-ever U.S. Clinical Investigation of iPSC-derived Cell Product

FT500 to be Featured in Oral Presentation on Monday, December 3 at ASH Annual Meeting

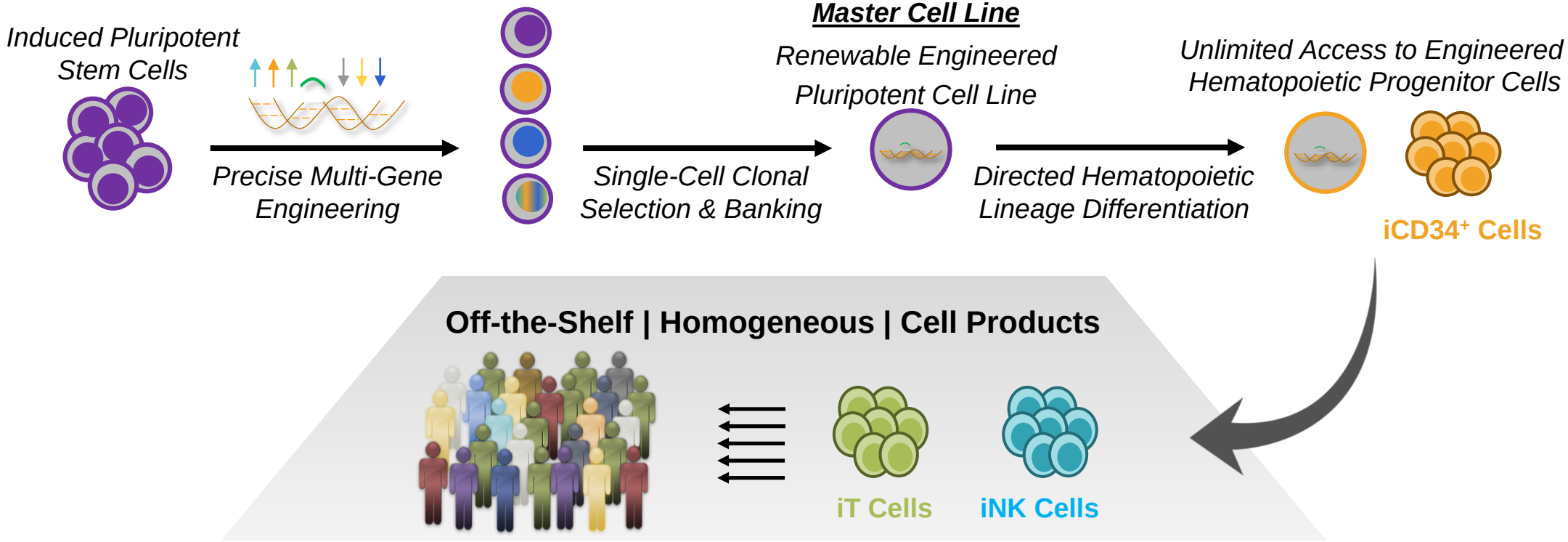
San Diego, CA – November 30, 2018 – Fate Therapeutics, Inc. (NASDAQ: FATE), a clinical-stage biopharmaceutical company dedicated to the development of programmed cellular immunotherapies for cancer and immune disorders, announced today that the U.S. Food and Drug Administration (FDA) has allowed its Investigational New Drug (IND) Application for FT500, the Company's universal, off-the-shelf natural killer (NK) cell product candidate derived from a clonal master induced pluripotent stem cell (iPSC) line. The clinical trial of FT500 is expected to be the first-ever clinical investigation in the U.S. of an iPSC-derived cell product.

iPSC Platform & Pipeline Overview

Bob Valamehr, PhD, Chief Development Officer

iPSC Product Platform for Off-the-Shelf Cell Products

iPSC-derived Cell-based Cancer Immunotherapies



Does not require patient-sourced cells

Eliminates stochastic editing variability associated with pool engineering

Consistent, reliable and cost-effective product forms

Unprecedented scalability

Off-the-shelf production of cells

Addresses Critical Limitations of Patient-Sourced Cellular Therapies

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Genetic Engineering / Editing

Challenges using Patient- and Donor-derived Cells

Not All Cells Are Engineered

Gene Edit Technology	CRISPR/Cas9	ZFN	TALEN
Gene Edit Tool Delivery	RNP	mRNA	mRNA
CAR Transduction	AAV6	AAV6	Unknown
TRAC-	97% / ~98%	93%	97%
β2M-	76% / 83%	96%	91%
CAR+ in TRAC	61% / 64%	77%**	69%**
PD1-	97%	----	----
CISH-	----	93%	----
TRAC- / β2M-	74%* / >80%	91%	89%
TRAC- / β2M- / CAR+ in TRAC	47%* / ~50%	70%*	61%*
TRAC- / β2M- / CAR+ in TRAC / PD1-	46% / 48%*	----	----
TRAC- / β2M- / CAR+ in TRAC / CISH-	----	65%*	----
TRAC- / β2M- / CAR+ in TRAC / NKi in β2M	----	----	42%*

Source: Guggenheim Securities

Not All Engineered Cells Are Pristine

- Random integration of transgenes
- Double stranded breaks in DNA
- Genetic translocations
- Off-target editing

Disruption of normal cellular machinery ---> potential for abnormal expression patterns and oncogenesis

The need for a true off-the-shelf cellular platform to compliment advancing engineering technologies and reduce the inherent variability & risk associated with cellular manufacturing

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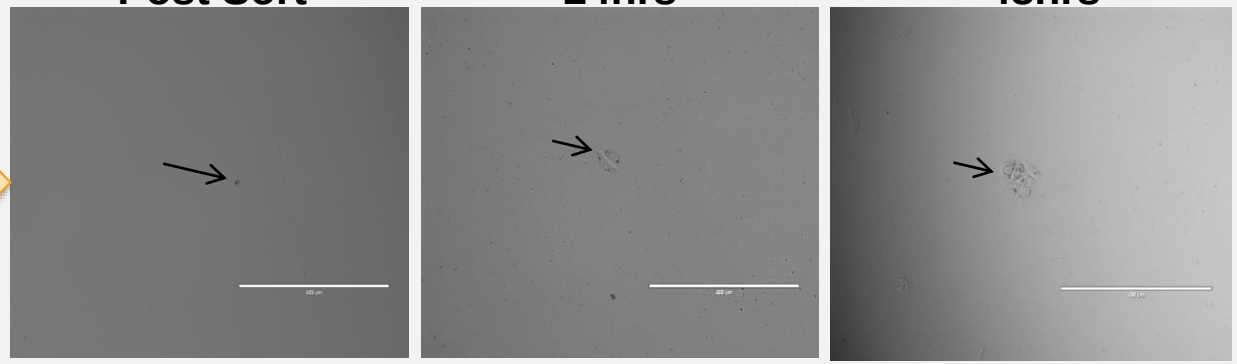
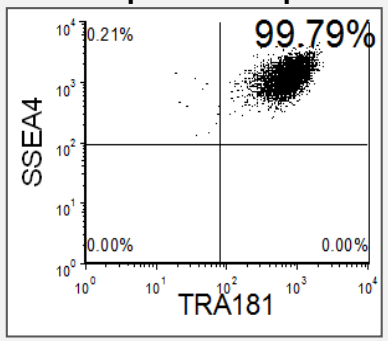
Foundation of iPSC Product Platform

Derivation & Selection of Renewable Master iPSC Clone with Preferred Properties

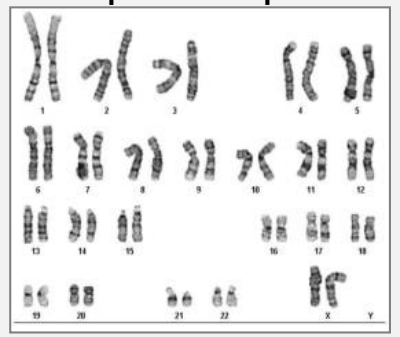
- Reprogram
- Gene Edit
- Single Cell Sort



Homogeneous Population at p25

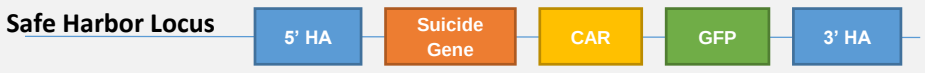


Karyotype Normal Population at p25

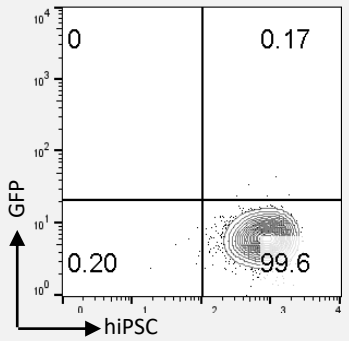


Valamehr et al 2012, 2013, 2014

Precise, Multi-Gene Insertion of hiPSC Clone

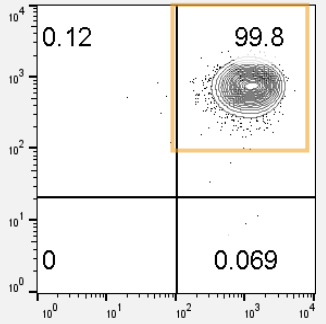


Parental Line



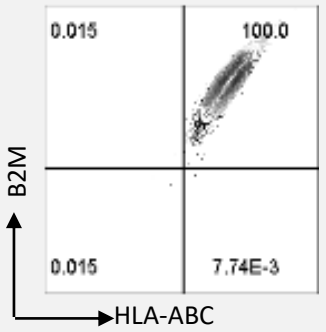
Cassette KI

Engineered Clonal Line



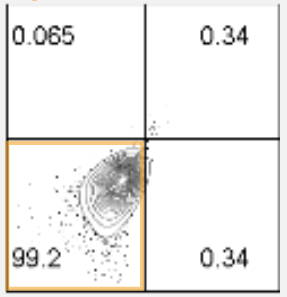
Precise Genetic Disruption in hiPSC Clone

Parental Line



B2M KO

Engineered Clonal Line



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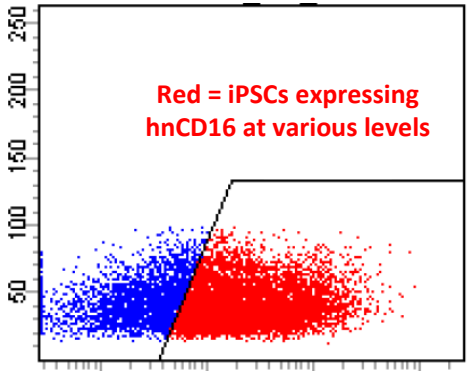
Selection of Renewable Master iPSC Clone (FT516)

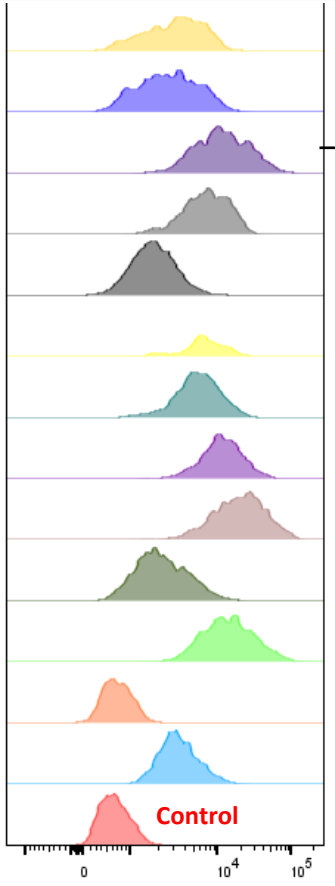
Unprecedented Ability for Single-cell Isolation, Characterization, Comparison and Selection

iPSC Transduction with hnCD16 Lentivirus



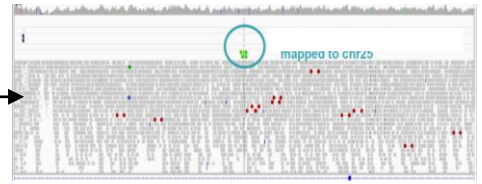
Single hnCD16 iPSC Clone into each well of 96-well plate

hnCD16 Expression Analysis of each iPSC Clone



Genome Sequencing of Selected hnCD16 iPSC Clone

Selected hnCD16 iPSC Clone



- ✓ **Determination of copy number**
- ✓ **Identification of exact integration site**
- ✓ **Confirmation of non-disruptive transgene integration**
- ✓ **Confirmation of clonality based on transgene integration signature**
- ✓ **A myriad of additional safety and efficacy analyses**

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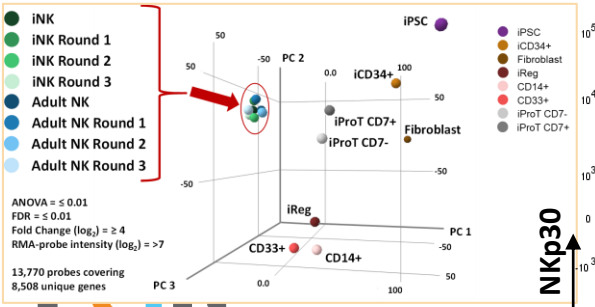
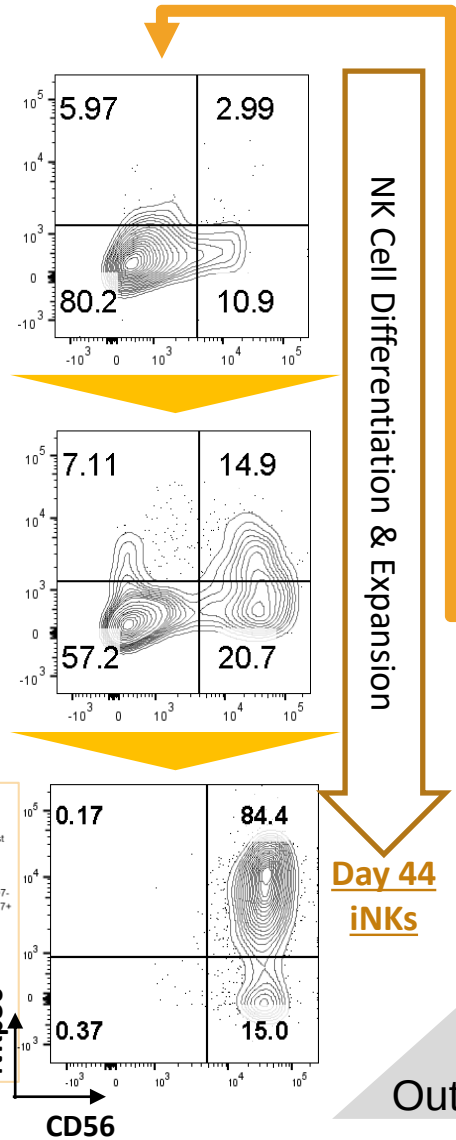
Production of Homogeneous Cell Products

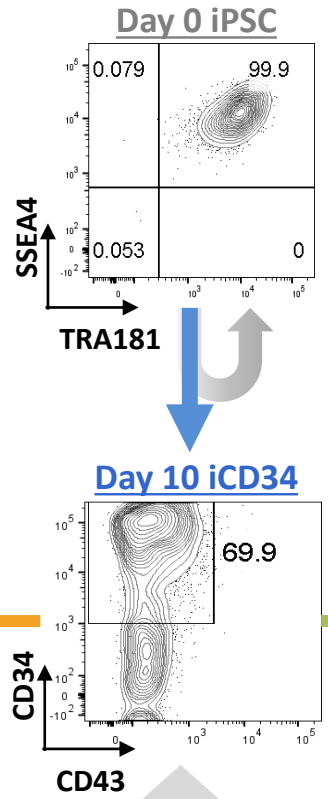
Consistent, Scalable and Cost-effective Manufacture from Renewable Master iPSC Clone

Clinical Manufacturing Underway @ UMN, Molecular and Cellular Therapeutics

Manufacture Launch @ MSKCC, Cell Therapy and Cell Engineering





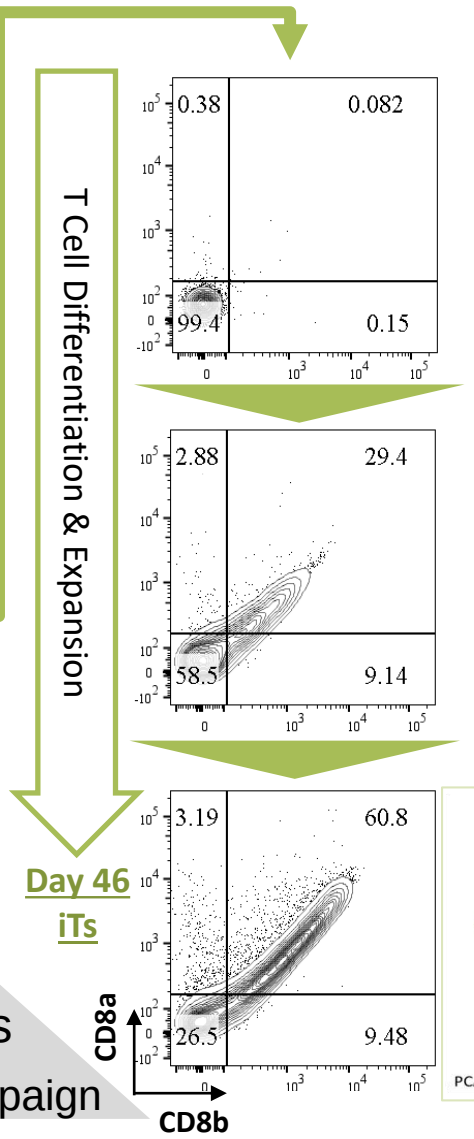


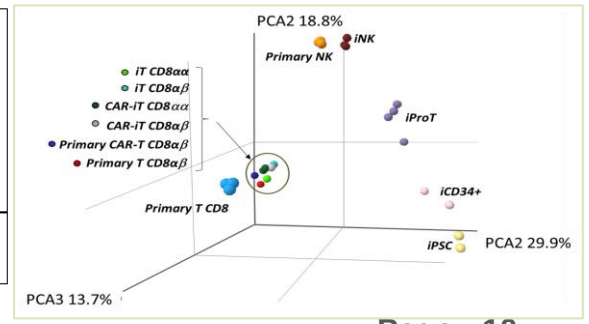
1x10^6 iPSCs

↓↓↓↓↓↓

1x10^{11} – 1x10^{12} iNKs/iTs

Output Per Manufacturing Campaign





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iPSC-derived, Off-the-Shelf Cancer Immunotherapy Pipeline

	Description	R&D	Preclinical Dev	Process Dev	Manufacturing	IND Filing	Phase 1
Off-the-Shelf NK Cells (FT5xx)							
FT500	Allogeneic iNK + Check Point Inhibitors						
FT516	hnCD16 iNK (ADCC) + monoclonal antibodies						
FT596	CAR19 + hnCD16 + mbIL15 CD19 CAR-NK | USE | CIP						
FT538	CD38 KO + hnCD16 + mbIL15 + Daratumumab						
FT576	CAR-BCMA + hnCD16 + CD38 KO +/- Daratumumab						
FT5solid	CARsolid + USE + CIP + multifaceted engineered attributes						
Off-the-Shelf T Cells (FT8xx)							
FT819	TCRless TRAC-Targeted CAR19						
FT896	TCRless TRAC-Targeted CAR19 + USE						
FT817	TCRless TRAC-Targeted CAR-BCMA						
FT8solid	TCRless + TRAC-CARsolid + USE + multifaceted engineered attributes						

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University of Minnesota Driven to Discover℠

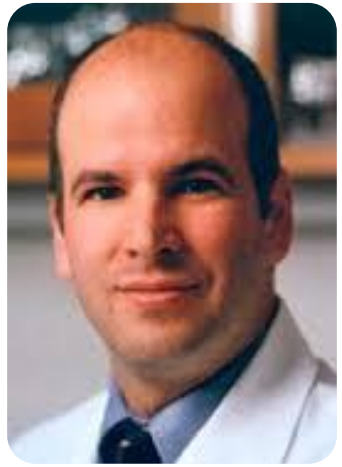
Oslo University Hospital

UC San Diego

Memorial Sloan-Kettering Cancer Center
The Best Cancer Care. Anywhere.

iPSC-derived, Off-the-Shelf Cell Products

Collaborations with Top Investigators and Leading Centers

Engineered NK Cells	CAR NK Cells	CAR T Cells
		
Jeffrey S. Miller, MD	***Dan Kaufman, MD PhD***	***Michel Sadelain, MD, PhD***
University of Minnesota Driven to Discover℠	UC San Diego	Memorial Sloan Kettering Cancer Center

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FT500 + CPB: Bridging Innate and Adaptive Immunity

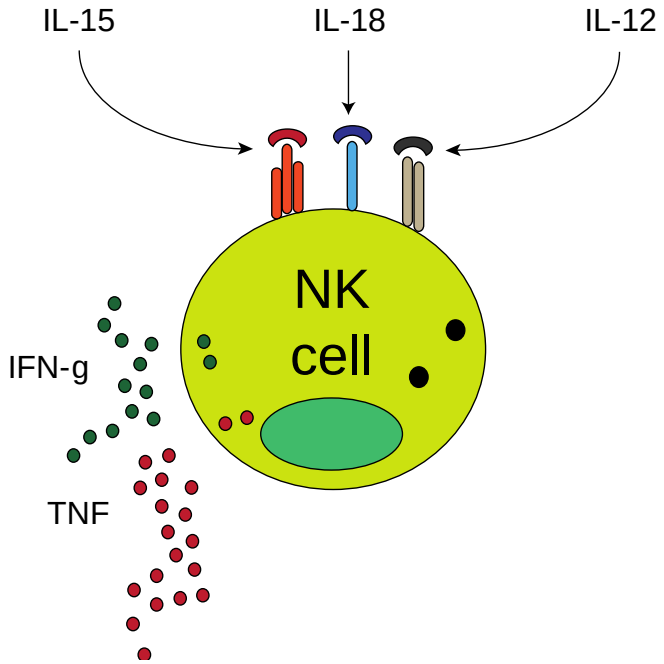
Jeffrey S. Miller, MD

Masonic Cancer Center
University of Minnesota

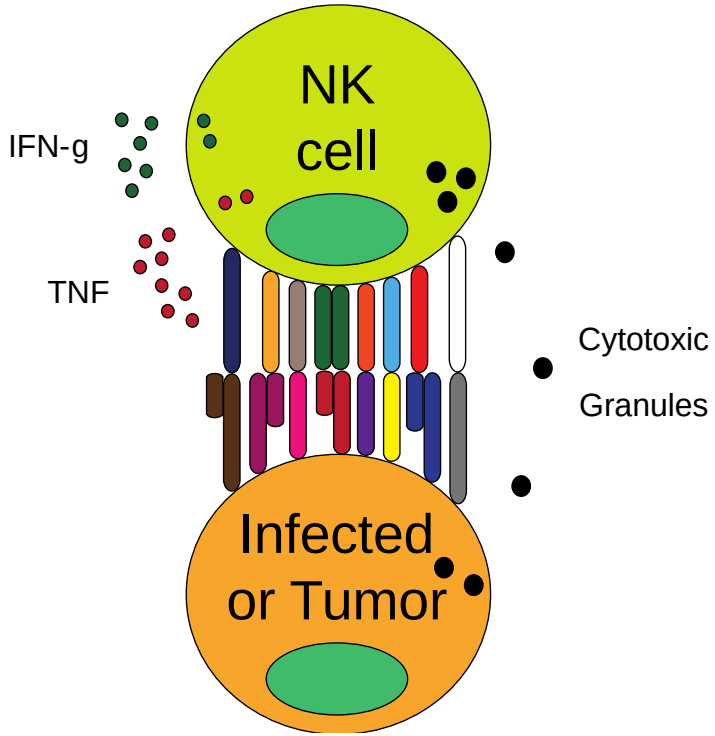
NK Cell Biology

Multifaceted Mechanisms of Anti-Tumor Activity

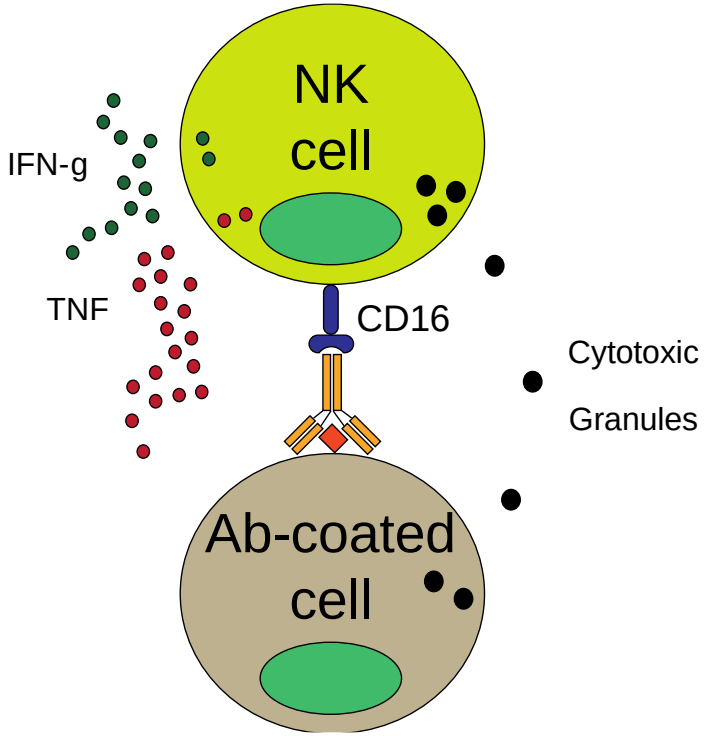
Cytokine Stimulation



Natural Cytotoxicity

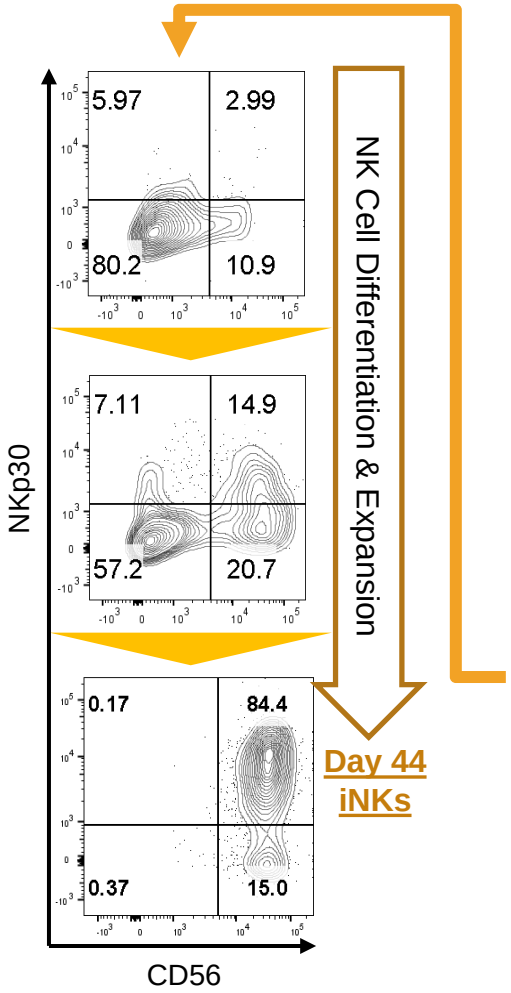


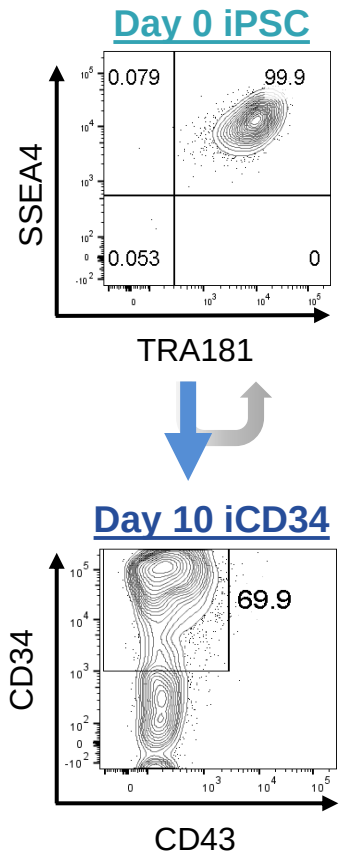
Antibody-Dependent Cellular Cytotoxicity (ADCC)

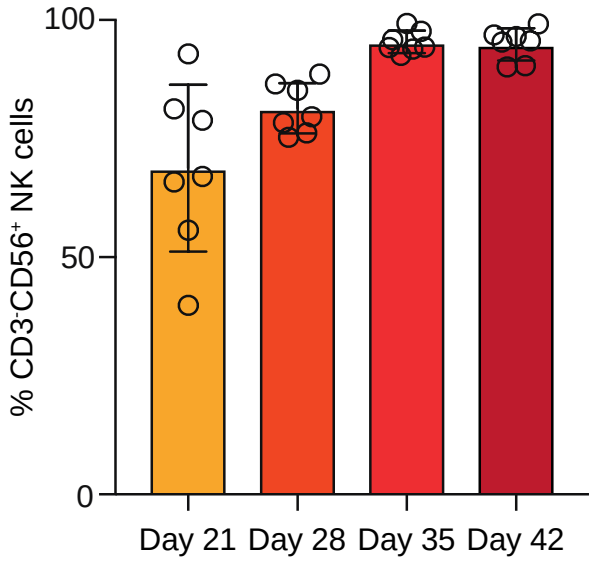


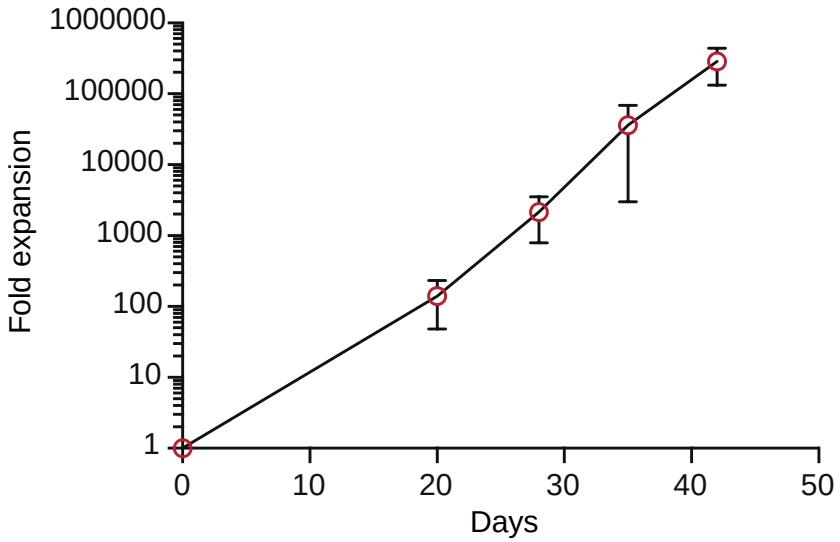
iPSC-derived, Off-the-Shelf NK Cells

Differentiation and Expansion from Clonal Master iPSC Line





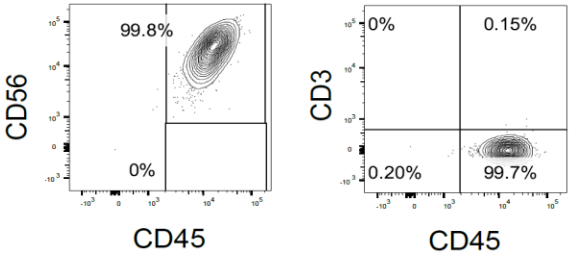




5L Grex

iNK Product

Phenotype of Thawed Product



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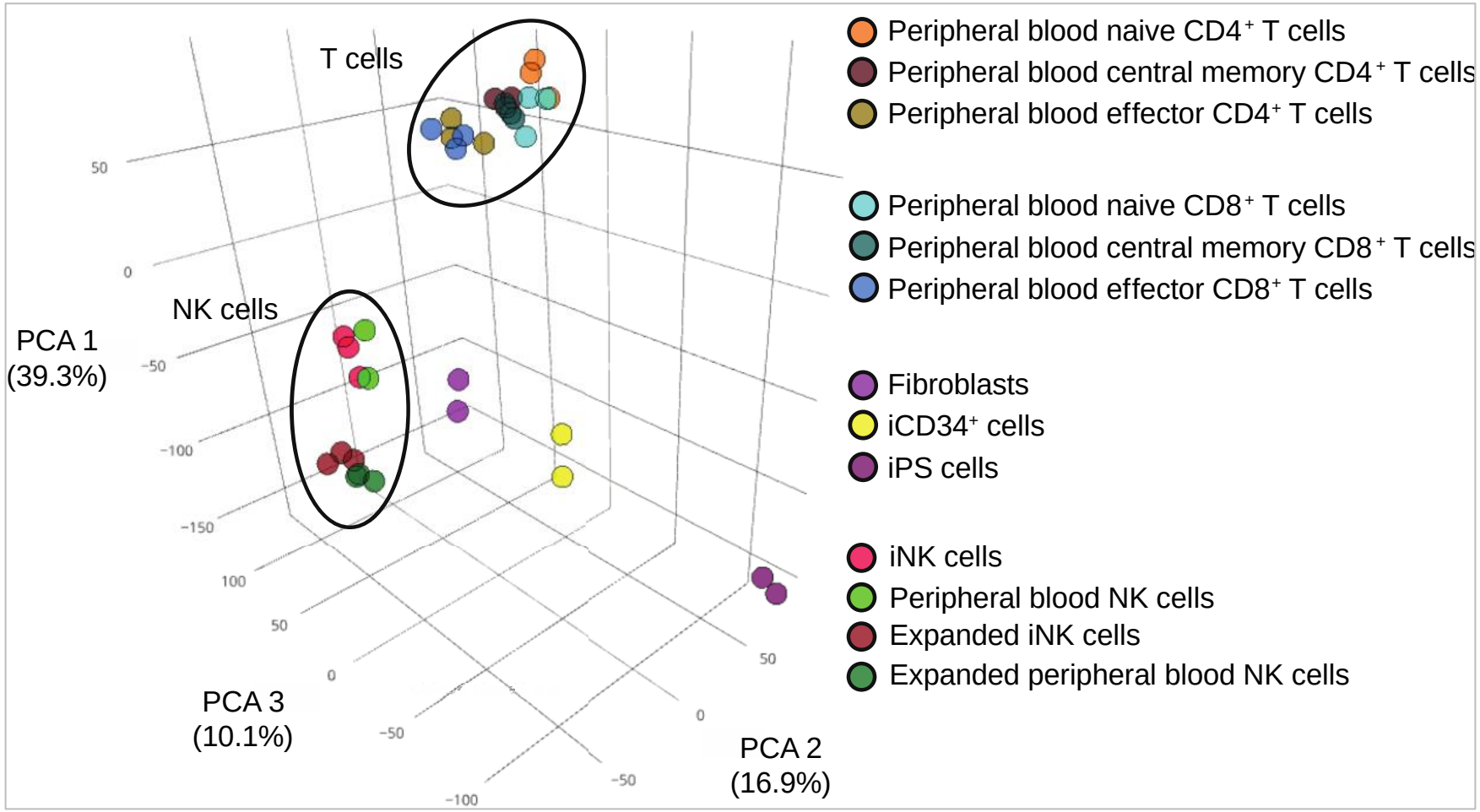
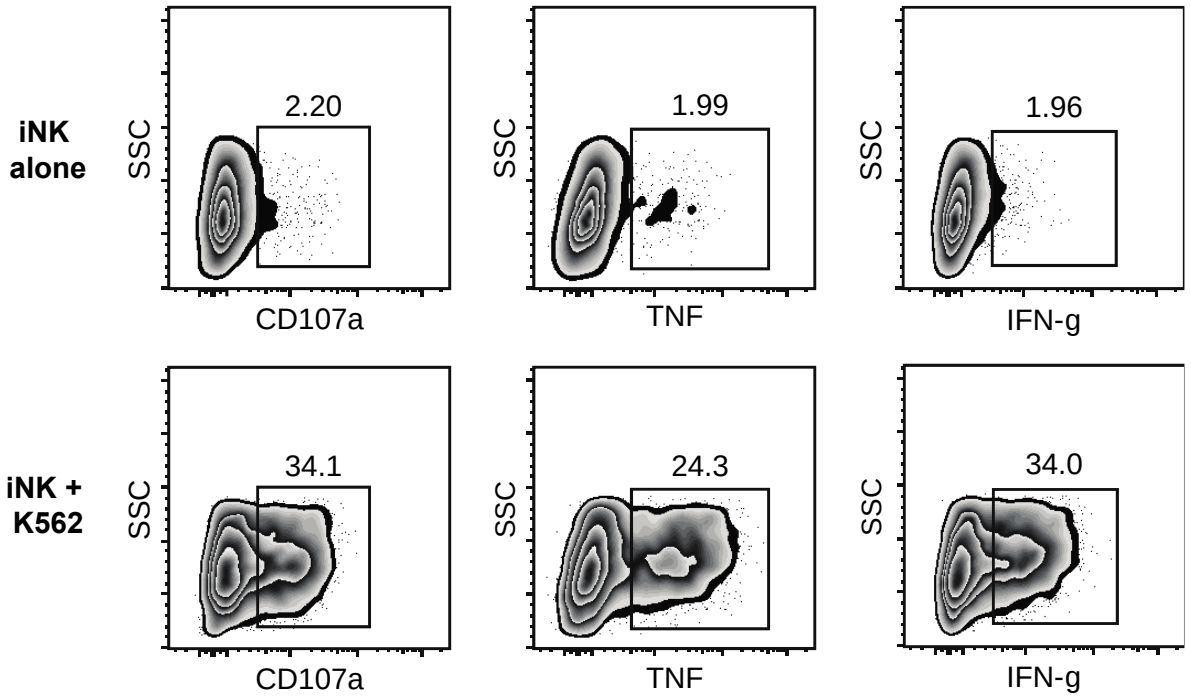
iNK Cell Characterization

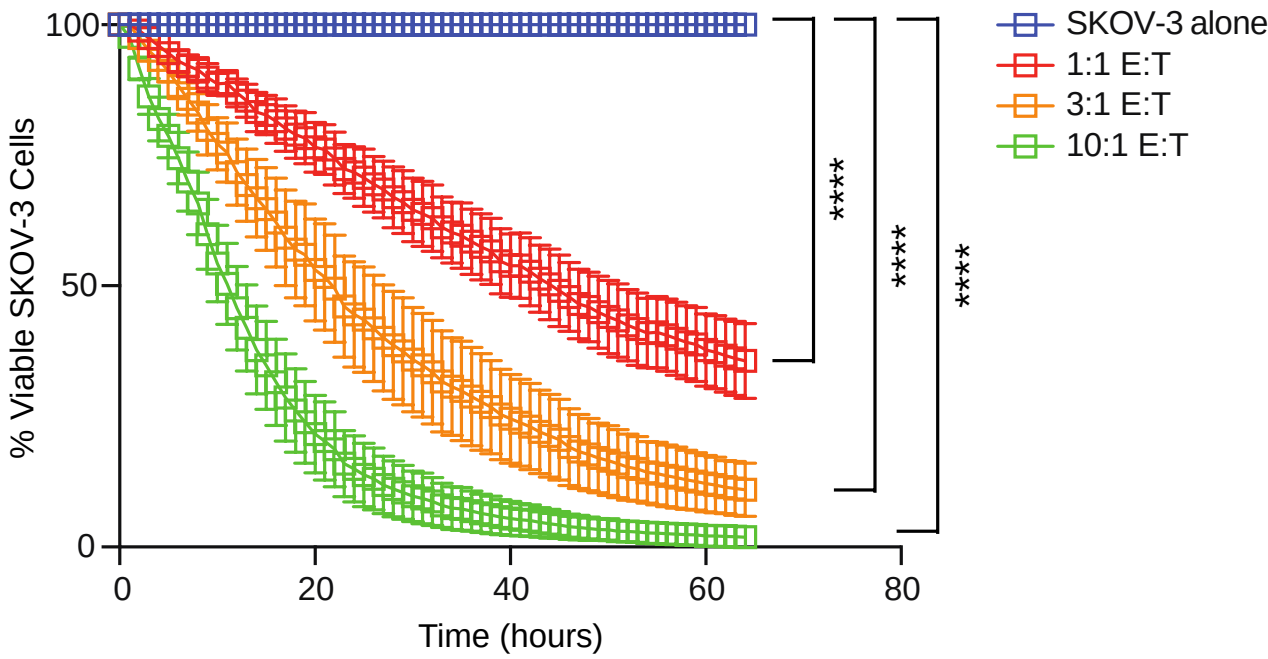
Transcriptome Similar to Primary Peripheral Blood NK cells



iNK Cell Cytotoxicity

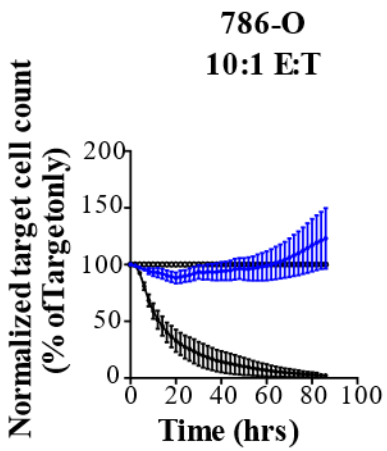
Robust Cytotoxic Function and Inflammatory Cytokine Production

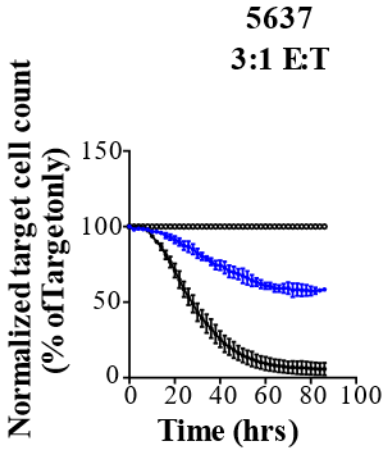


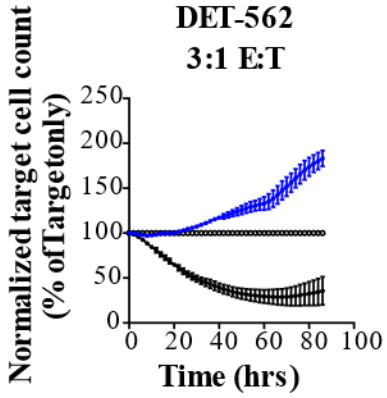


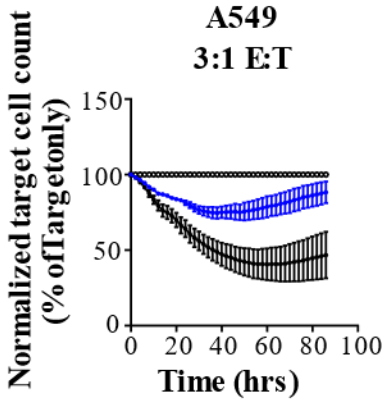
iNK Cell Cytotoxicity

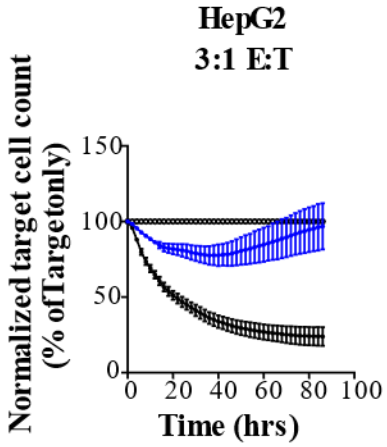
Demonstration of Enhanced Cytotoxicity Against Various Solid Tumors

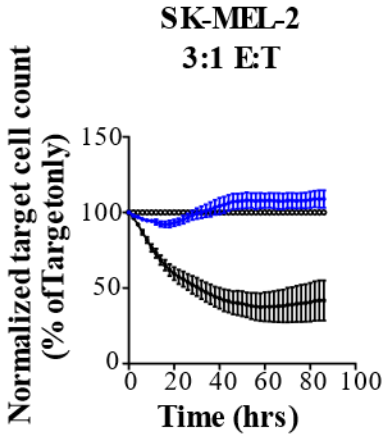


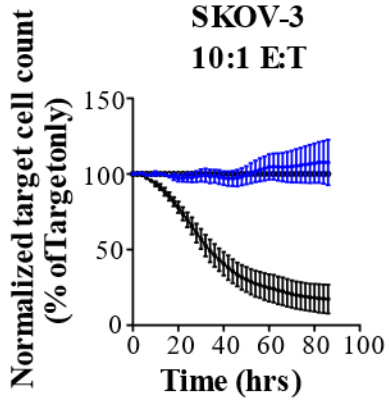


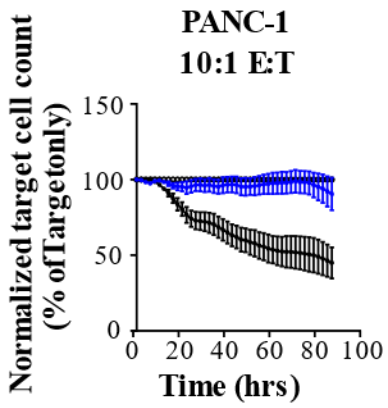










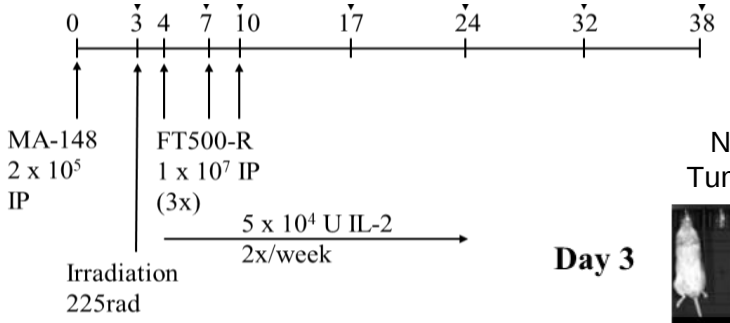


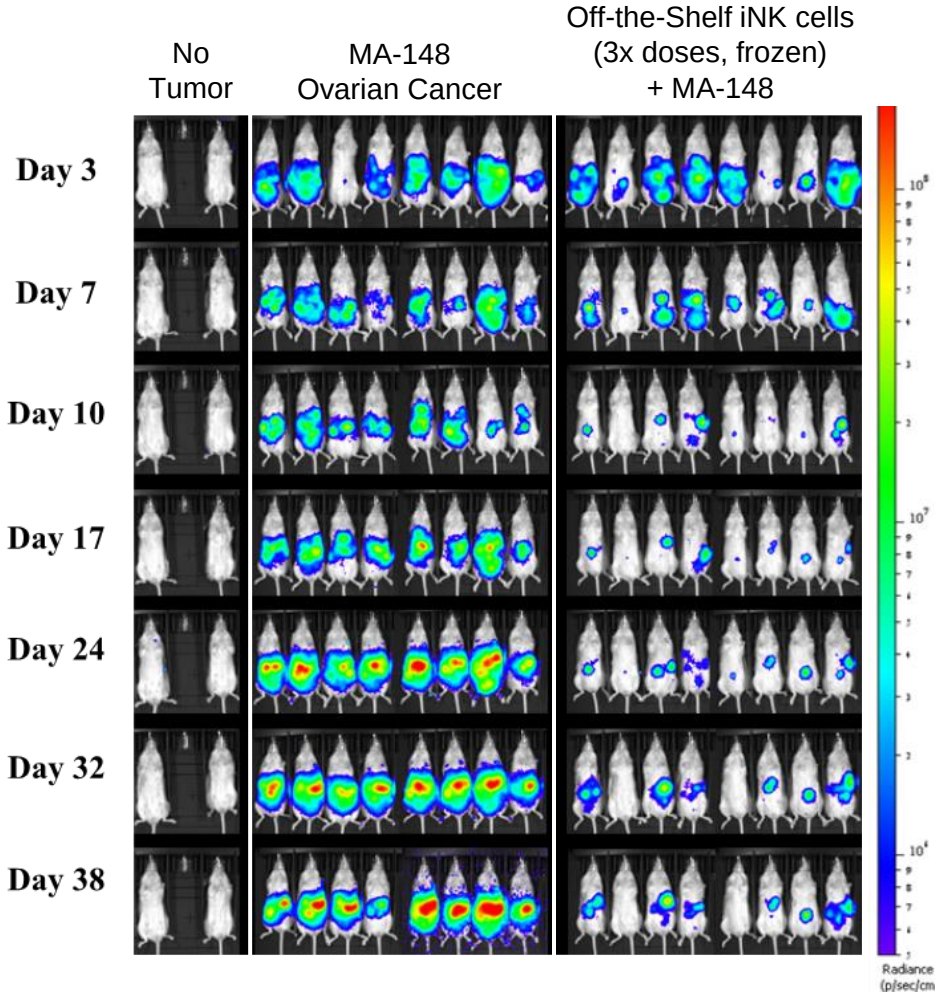
Blue circles = overnight primed peripheral blood-derived NK cells

Black circles = FT500

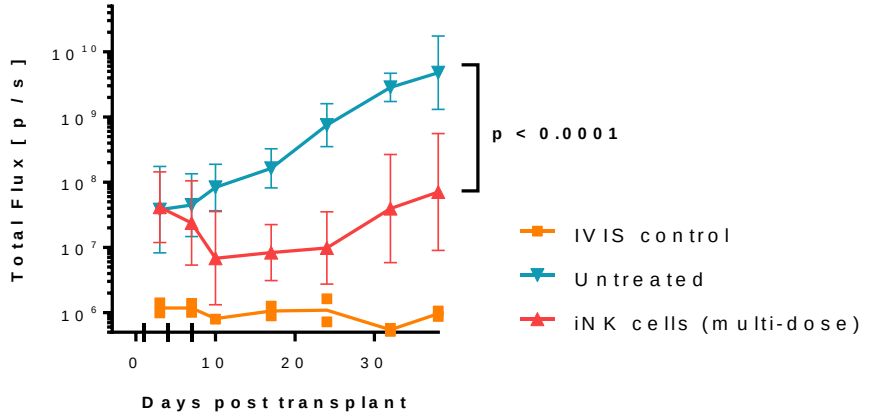
iNK Cell Cytotoxicity

In Vivo Anti-Tumor Function Using Multi-Dose Administration

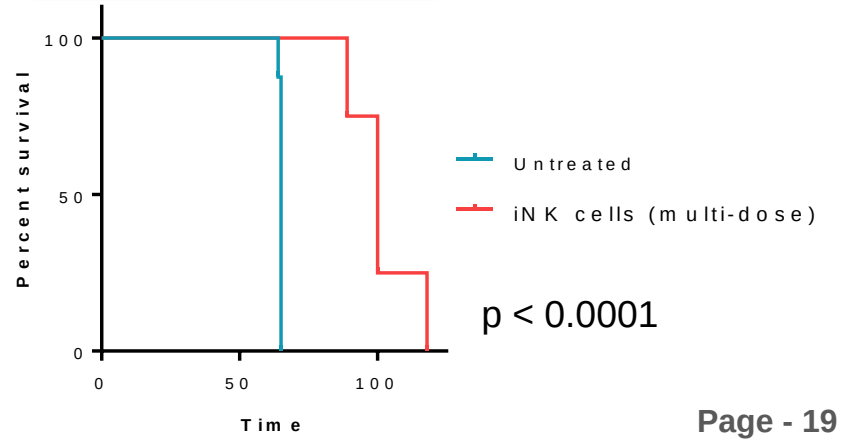




Tumor Growth



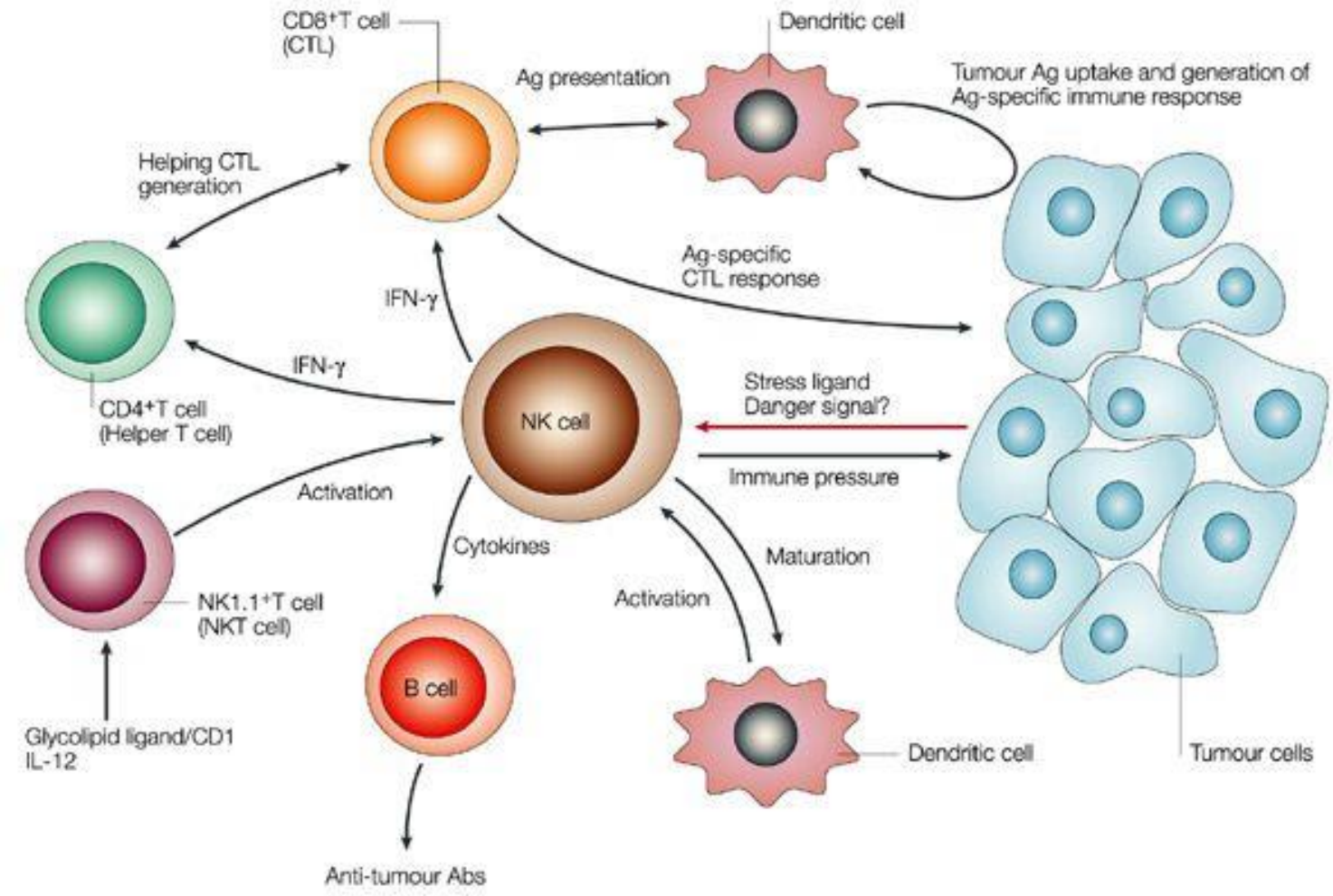
Survival



p < 0.0001

Unique Therapeutic Potential of NK Cells

Bridge Innate and Adaptive Immunity

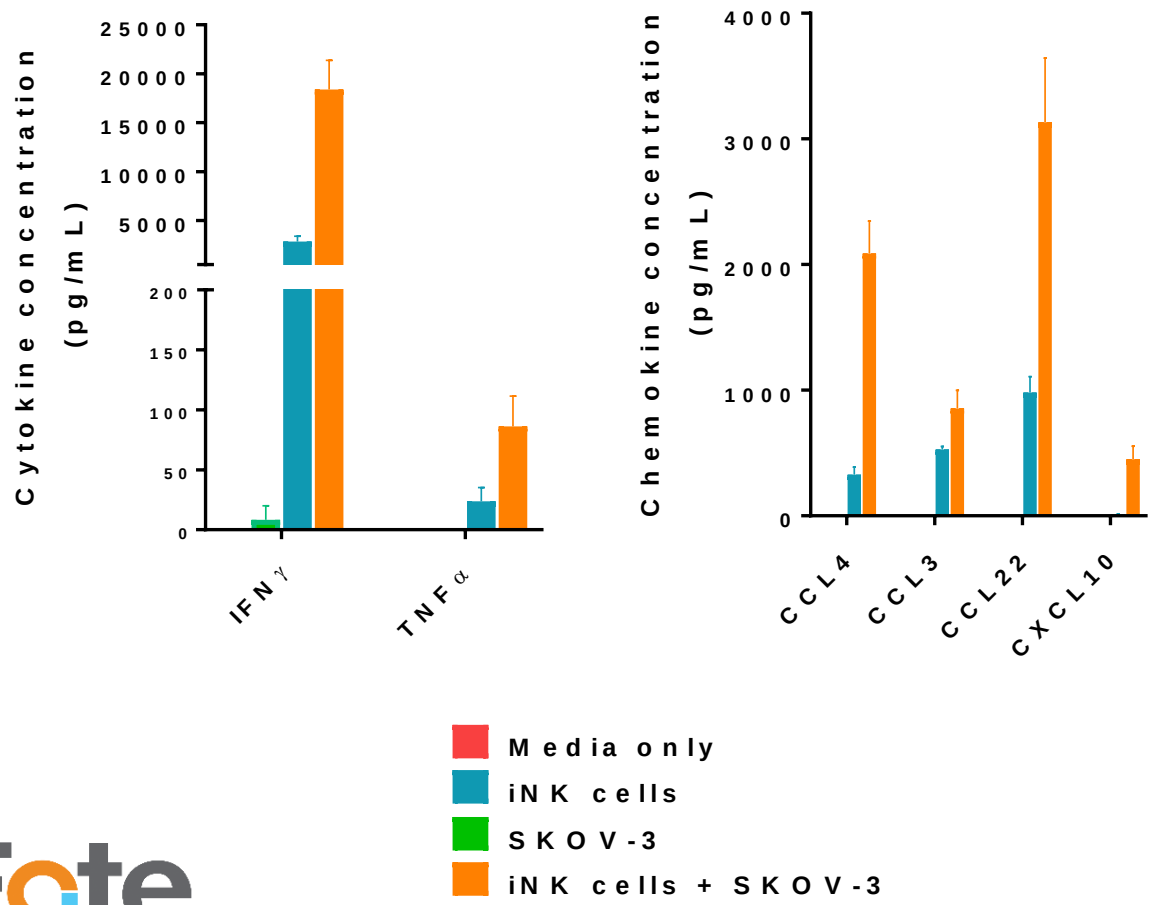


Nature Reviews | Cancer

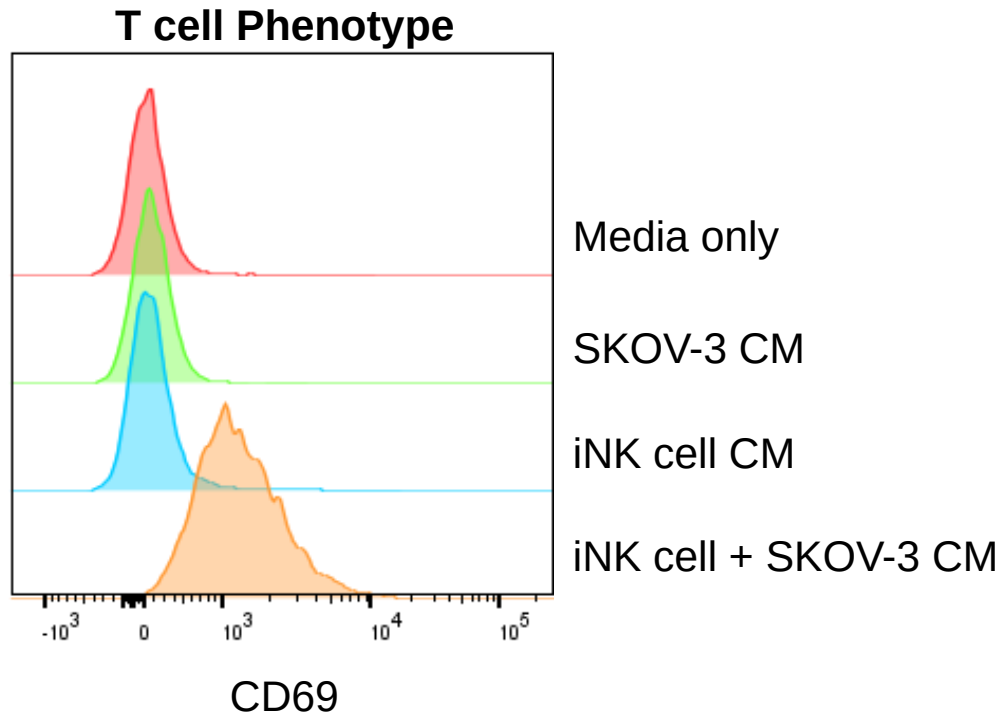
iNK Cells Induce Adaptive Immunity

Soluble Factors from iNK Cells Activate Cytotoxic T Cells

Cytokine and Chemokine Production by iNK cells



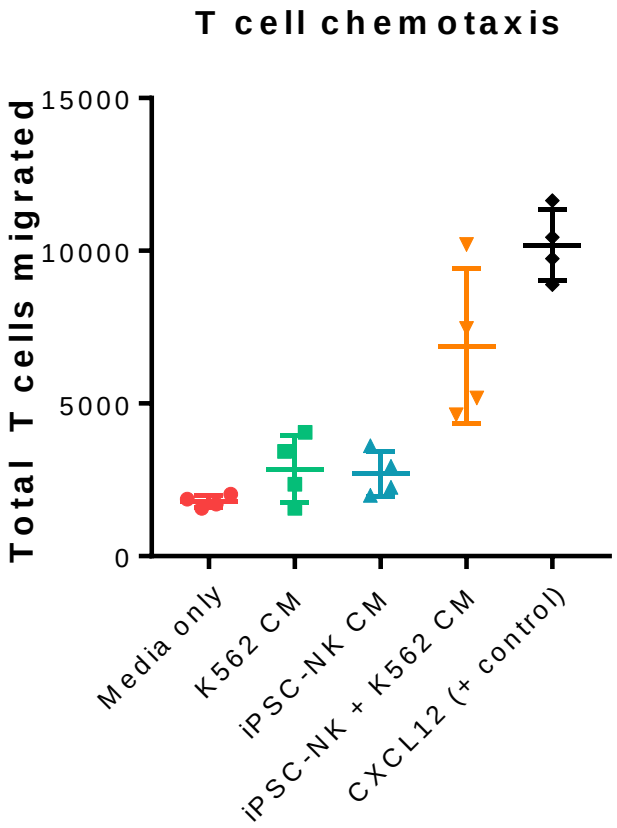
Conditioned Media-mediated T cell Activation



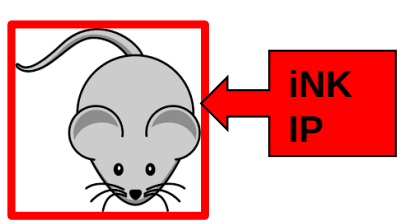
iNK Cells Induce Adaptive Immunity

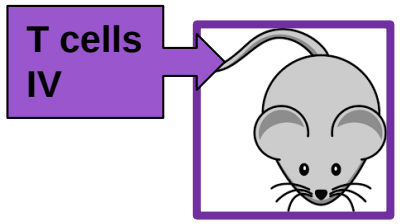
iNK Cells Promote T Cell Recruitment

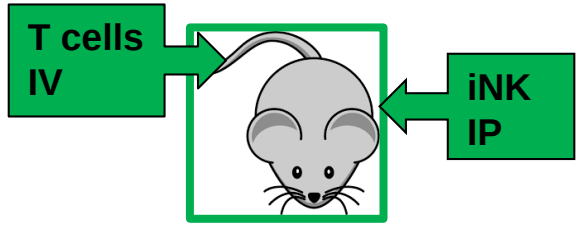
In Vitro Recruitment

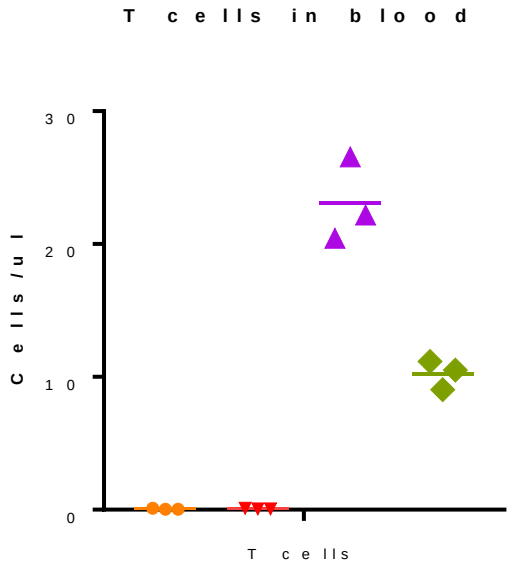


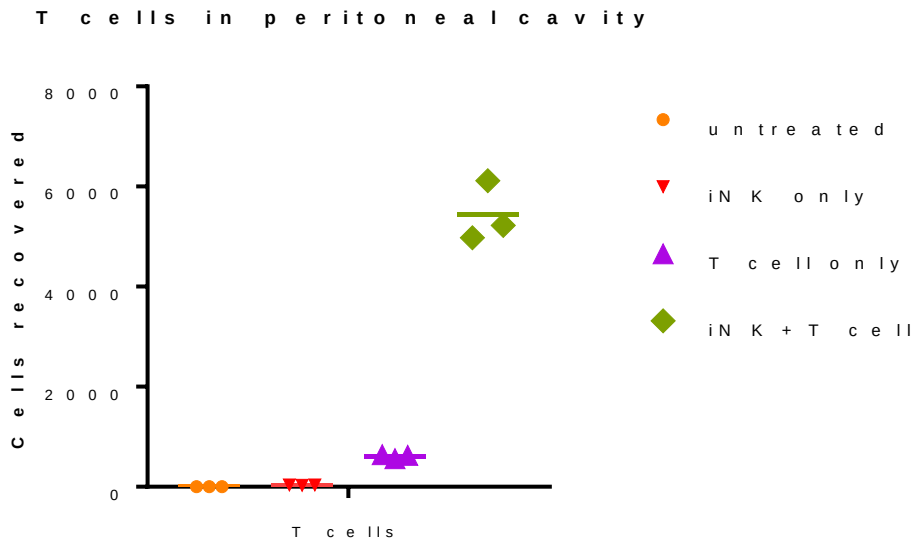
In Vivo Recruitment











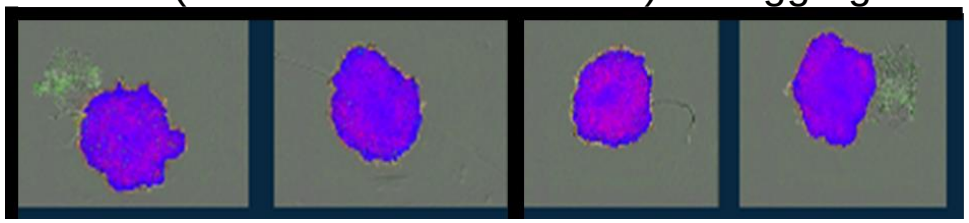
iNK Cells + T Cells + CPI Therapeutic Agent

Synergy Uniquely Drives Complete Killing of Tumor Spheroids

3-D Ovarian Cancer Tumor Model Setup

SKOV3 (Ovarian Cancer Derived) 3D Aggregates

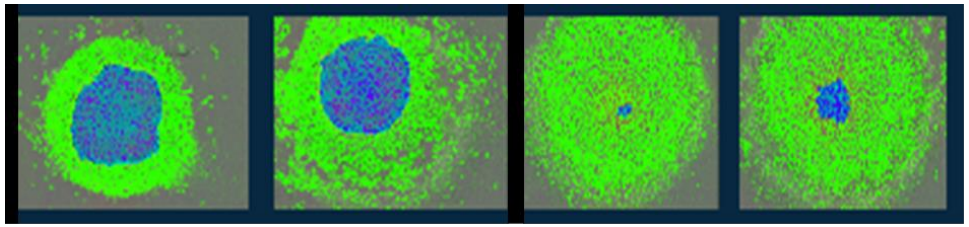
SKOV3



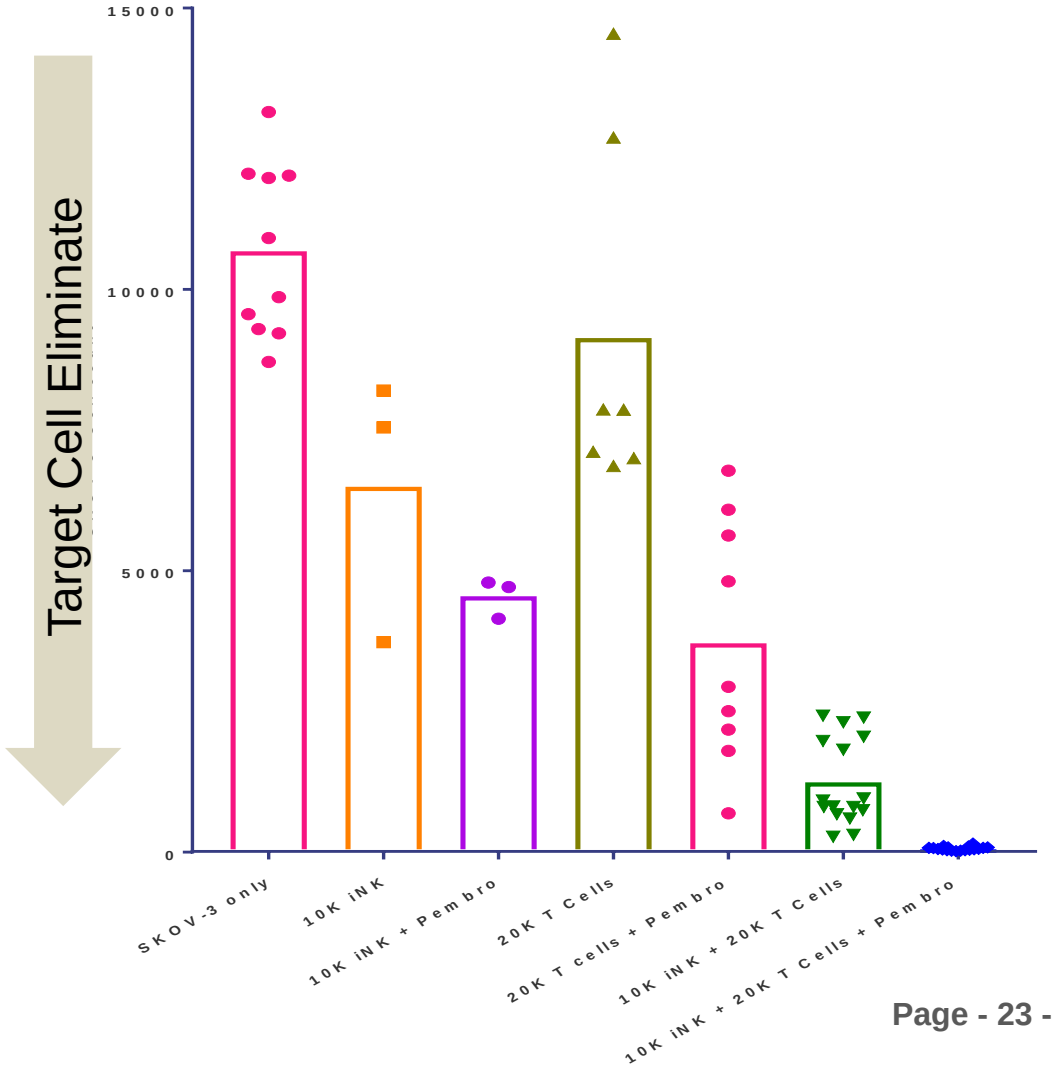
Add agents

Various Scenario

SKOV3
T cell



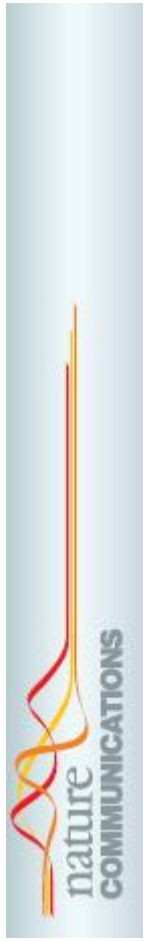
3-D Ovarian Cancer Tumor Model Readout



Fate THERAPEUTICS

FT500: iNK Cell Combination with Checkpoint Blockade

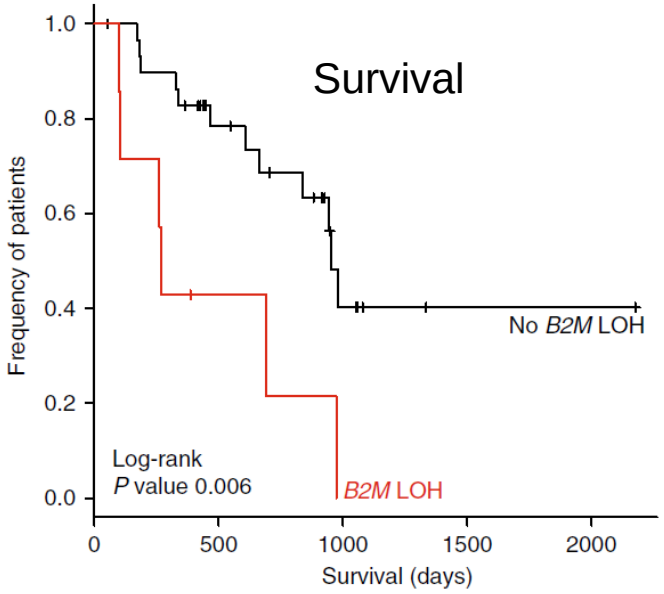
Rescue Therapy in Patients with B2M Mutations



Resistance to checkpoint blockade therapy through inactivation of antigen presentation

Moshe Sade-Feldman[1,2], Yunxin J. Jiao[2,3], Jonathan H. Chen[2,4], Michael S. Rooney[2], Michal Barzily-Rokni[1], Jean-Pierre Eliane[4], Stacey L. Bjorgaard[1,2], Marc R. Hammond[1], Hans Vitzthum[1], Shauna M. Blackmon[1], Dennie T. Frederick[1], Mehlika Hazar-Rethinam[1], Brandon A. Nadres[1], Emily E. Van Seventer[1], Sachet A. Shukla[2,5], Keren Yizhak[2], John P. Ray[2], Daniel Rosebrock[2], Dimitri Livitz[2], Viktor Adalsteinsson[2], Gad Getz[2,4], Lyn M. Duncan[4], Bo Li[6], Ryan B. Corcoran[1], Donald P. Lawrence[1], Anat Stemmer-Rachamimov[4], Genevieve M. Boland[7], Dan A. Landau[2,8,9], Keith T. Flaherty[1], Ryan J. Sullivan[1] & Nir Hacohen[1,2]

- *B2M* mutations are enriched in patients who are resistant to checkpoint therapy (~30%)
- Loss of *B2M* associated with poor survival
- MHC Class 1 null tumor cells are highly susceptible to killing by NK cells

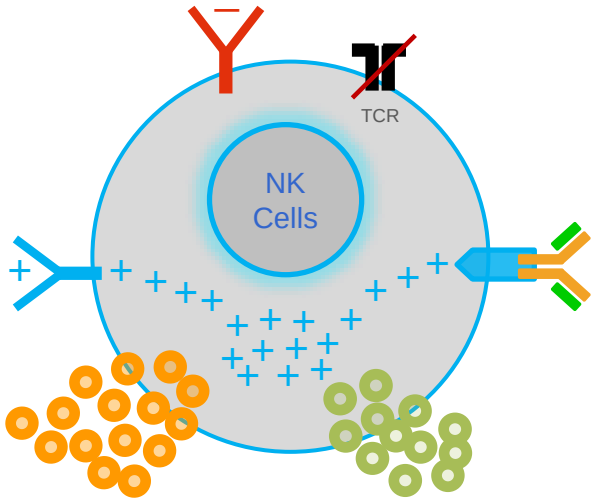


Fate THERAPEUTICS

FT500: iNK Cell Combination with Checkpoint Blockade

Landmark IND Cleared by FDA for Clinical Investigation of First iPSC-derived Cell Therapy

Multifaceted Function of NK cells



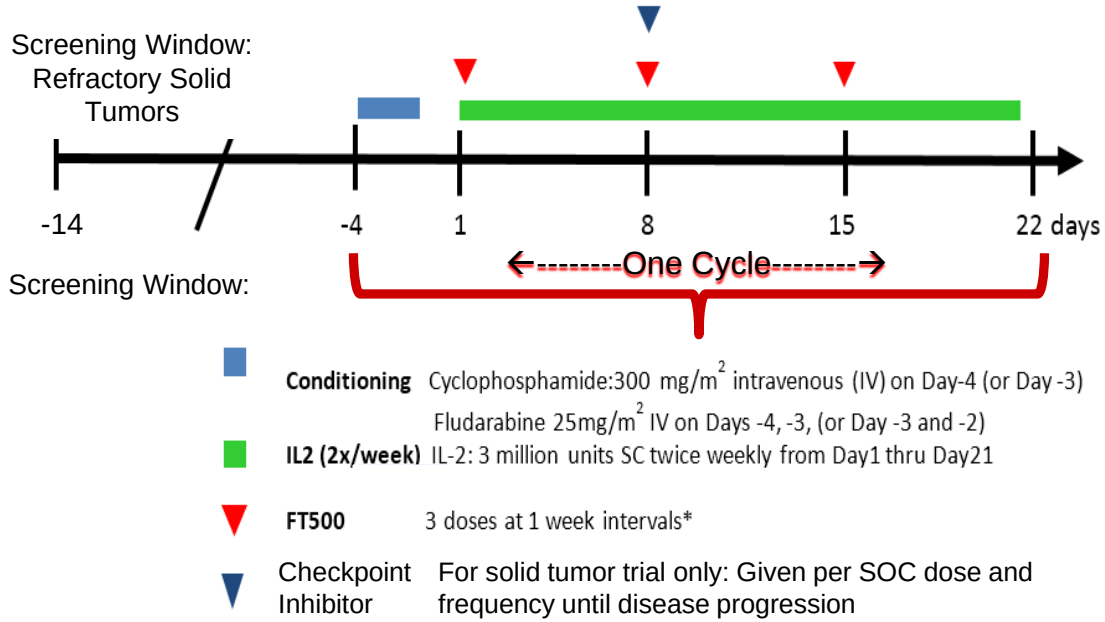
Secretion of pro-inflammatory cytokines and chemokines to recruit and activate the adaptive immune system

We have demonstrated that iNKs can:

- ✓ Activate primary T cells
- ✓ Support primary T cell infiltration and killing of 3-D tumor aggregates
- ✓ Support in vivo homing and trafficking of primary T cells
- ✓ Support synergistic killing of target cells when combined with primary T cells and PD1 checkpoint inhibitor

FT500 Clinical Trial Schema:

Multiple Cycles of FT500 + Checkpoint Inhibitor Dosed Weekly after Outpatient Lympho-Conditioning Regimen



Fate THERAPEUTICS

Enhancing CD16 and CAR Biology for NK cells

Dan S. Kaufman, MD PhD

UC San Diego

iPSC-derived NK Cell Tumor Targeting

Hematopoietic colony-forming cells derived from human embryonic stem cells

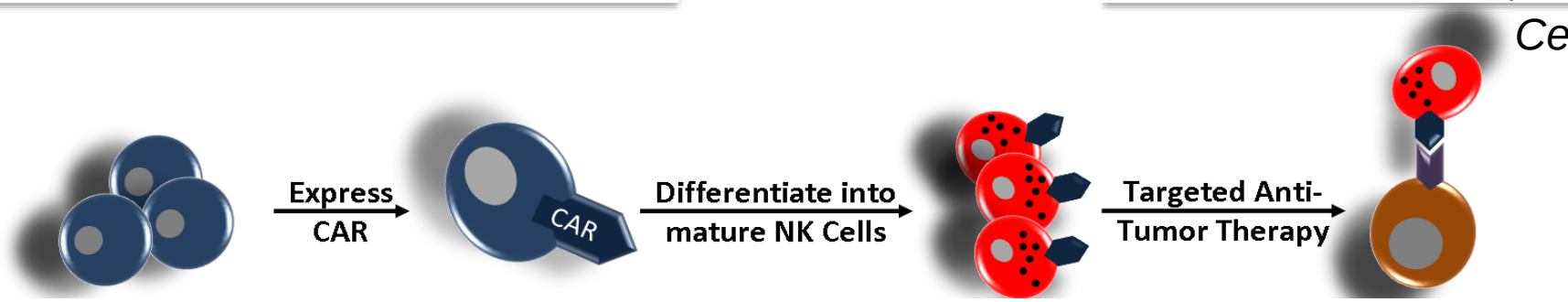
Dan S. Kaufman*, Eric T. Hanson†, Rachel L. Lewis†, Robert Auerbach‡, and James A. Thomson†§¶

PNAS, 2001

Human iPSC-Derived Natural Killer Cells Engineered with Chimeric Antigen Receptors Enhance Anti-tumor Activity

Ye Li,[1] David L. Hermanson,[2,4] Branden S. Moriarity,[3] and Dan S. Kaufman[1,5,*]

Cell Stem Cell, 2018



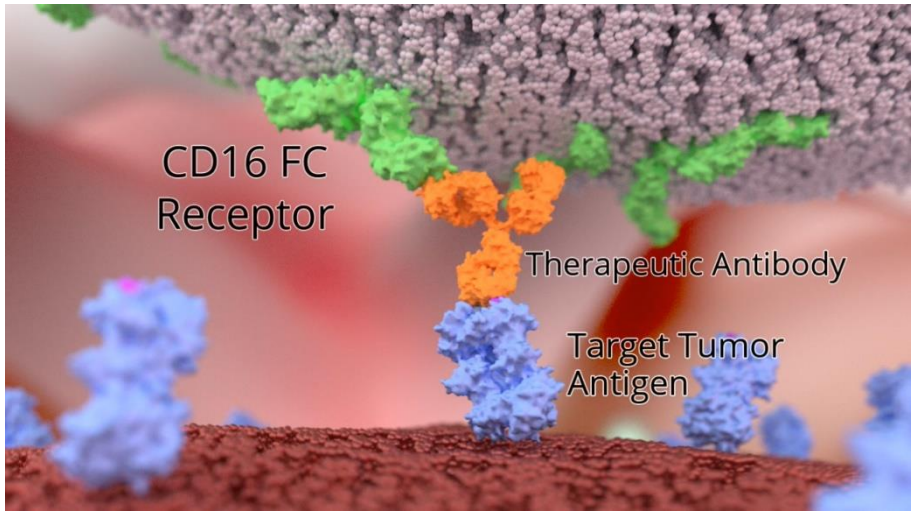
- **Advantages working with iPSCs as opposed to primary-derived cells from each patient**
  - Homogeneous starting cell population
  - Can obtain ~100% CAR-expressing cells
  - Potentially more potent effector cells with multiple engineering steps
  - Defined donor genetic makeup
  - Can target insertion
  - Potential for in depth preclinical testing

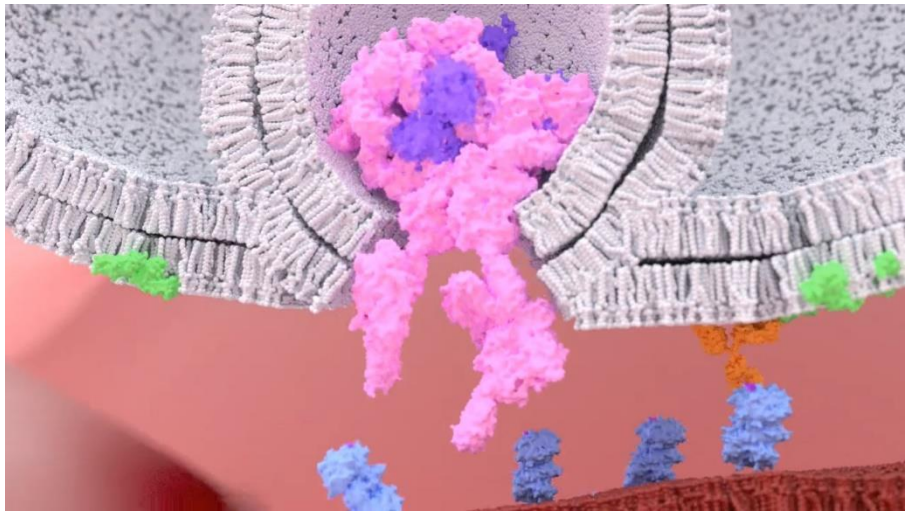
Fate THERAPEUTICS

Antibody Dependent Cellular Cytotoxicity (ADCC)

Mediated by NK Cells

- Antibody binds to tumor target via Fab and to Fc receptor on NK cells (CD16) via Fc, initiating release of perforins / granzyme resulting in tumor cell death





- ADCC contributes to anti-tumor activity of many FDA-approved antibodies
  - Herceptin, Erbitux, Rituximab, Darzalex, etc.

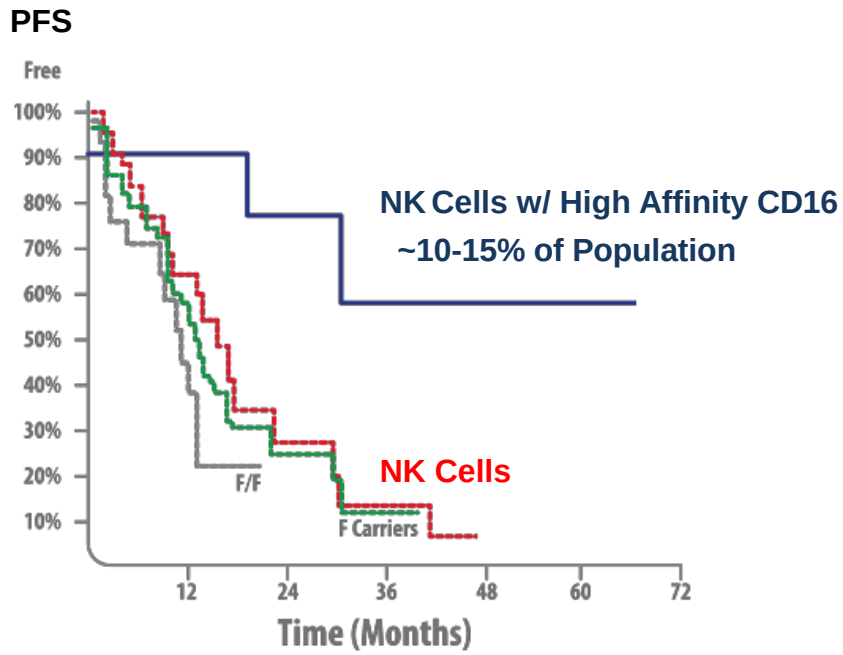
Fate THERAPEUTICS

ADCC: Clinical Proof-of-Concept

Enhanced ADCC Mediated by High Affinity CD16 Polymorphism Correlates with Improved Outcomes

Herceptin

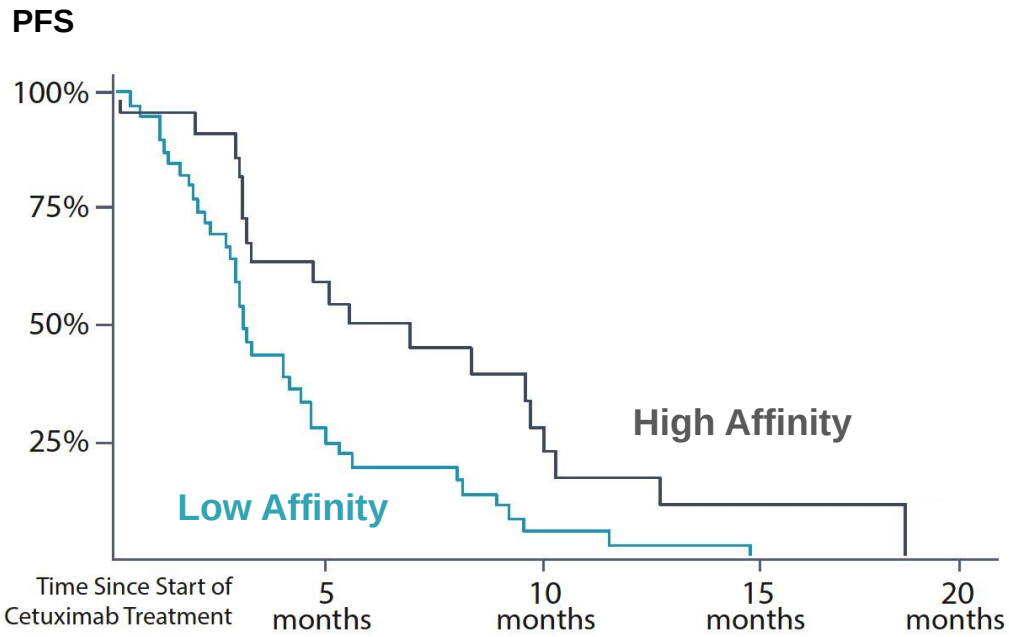
Metastatic Breast Cancer



Musolino et al, J. Clin Oncol, 26, 1789, 2008

Erbitux

Colorectal Cancer



Bibeau et al, J. Clin Oncol, 27, 1122, 2009

FT516: Engineered hnCD16 iNK Cell Product Candidate

Off-the-Shelf Cornerstone Approach for Multi-Targeting of Liquid & Solid Tumors

PLOS ONE

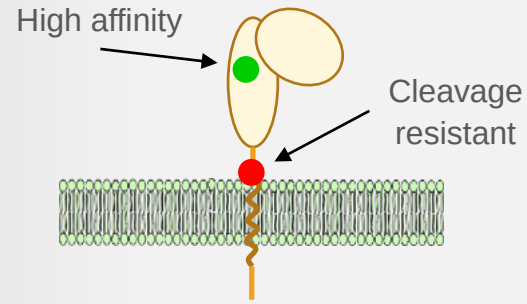
RESEARCH ARTICLE

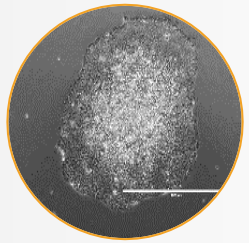
Identification of an ADAM17 Cleavage Region in Human CD16 (FcγRIII) and the Engineering of a Non-Cleavable Version of the Receptor in NK Cells

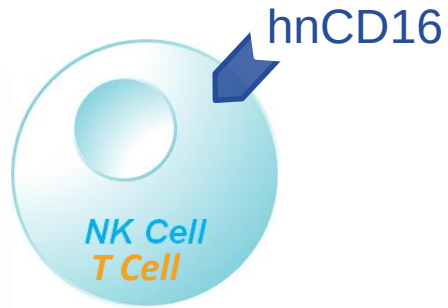
Yawu Jing[1], Zhenya Ni[2], Jianming Wu[1], LeeAnn Higgins[3], Todd W. Markowski[3], Dan S. Kaufman[2], Bruce Walcheck[1]*

Engineered high-Affinity non-Cleavable CD16 Fc Receptor

Modified form of CD16a IgG antibody-binding receptor resists shedding upon activation







Renewable Engineered Pluripotent Cell Line

Engineered hnCD16 iNK or iT Cells for Enhanced ADCC

FDA-approved Monoclonal Antibodies

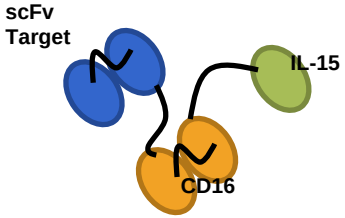
Rituxan Rituximab

Herceptin trastuzumab

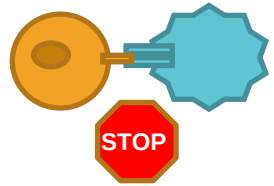
ERBITUX CETUXIMAB

DARZALEX

Bi- / Tri- Specific Engagers



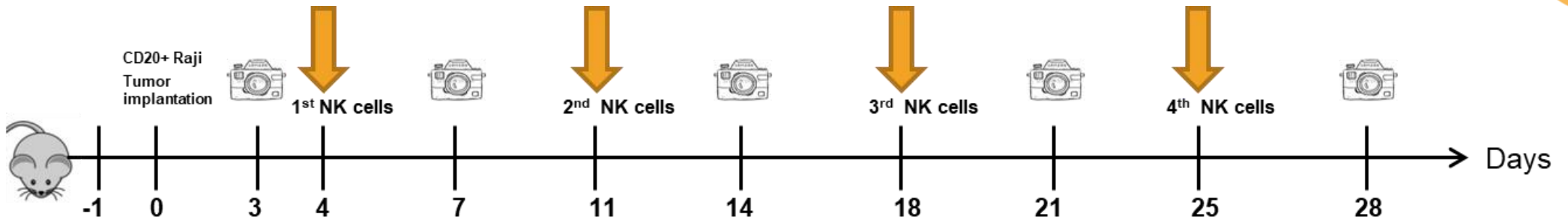
Checkpoint Inhibitors

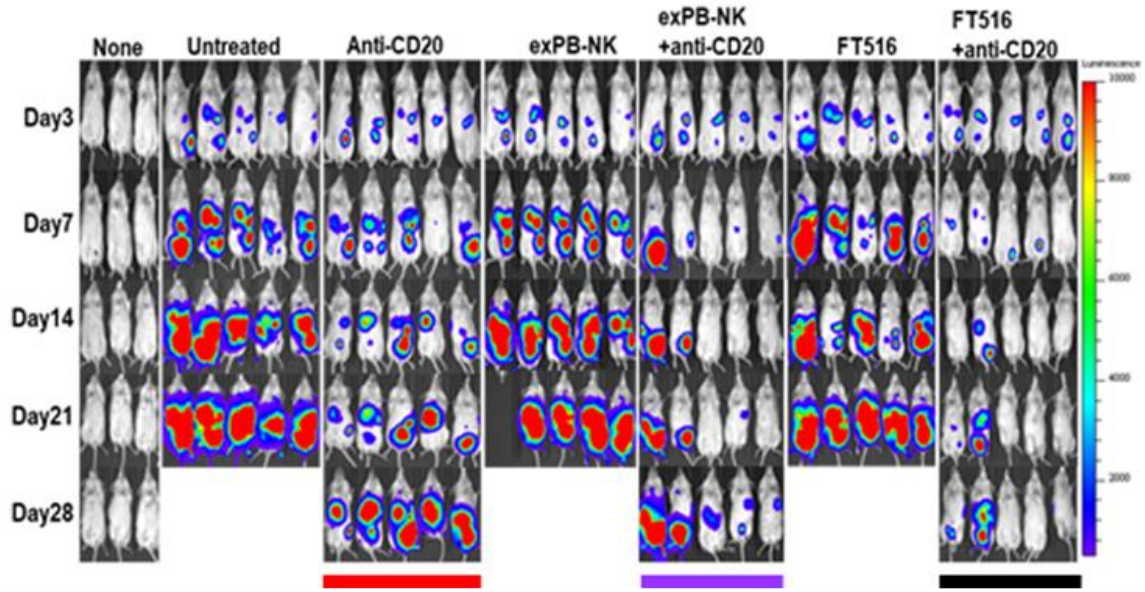


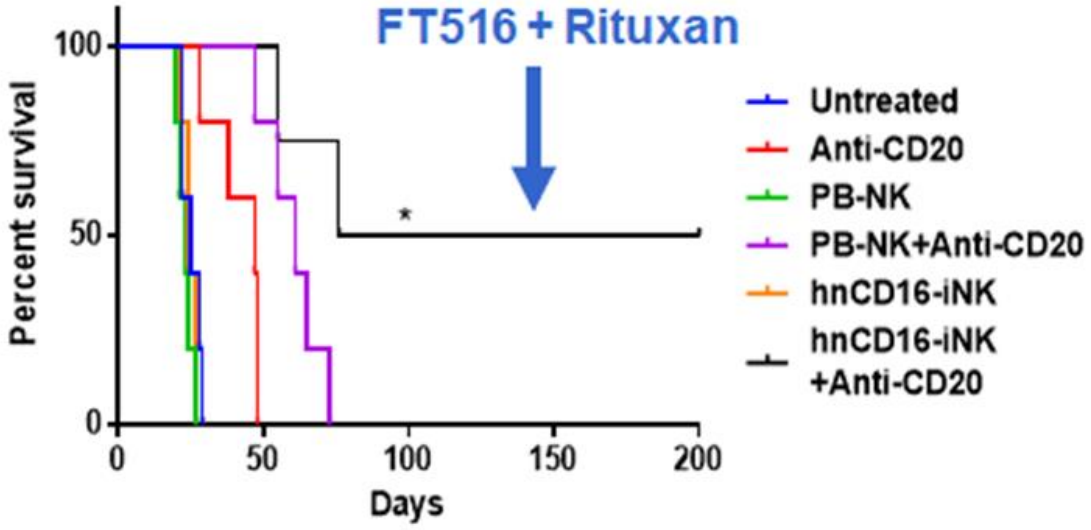
Chimeric Antigen Receptor

FT516: Combination with Rituxan

Promotes Enhanced In Vivo Survival

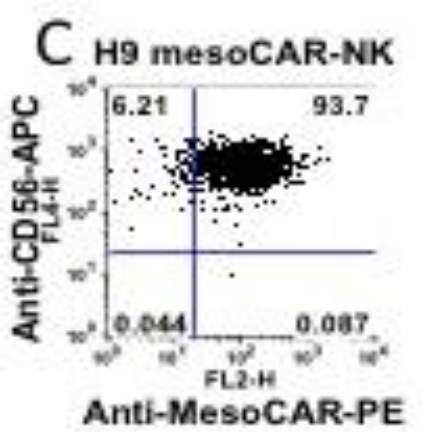






Chimeric Antigen Receptors (CARs) Designed for iNK Cells

- Initial studies used T-CAR construction in hESC/iPSC-NK cells



- Obtained good expression
  - >90% CAR-NK cells
  - Normal NK cell phenotype
  - Good function in vitro
  - T-CAR in NK cells had poor function in vivo

- Develop novel CARs specifically designed for NK cells

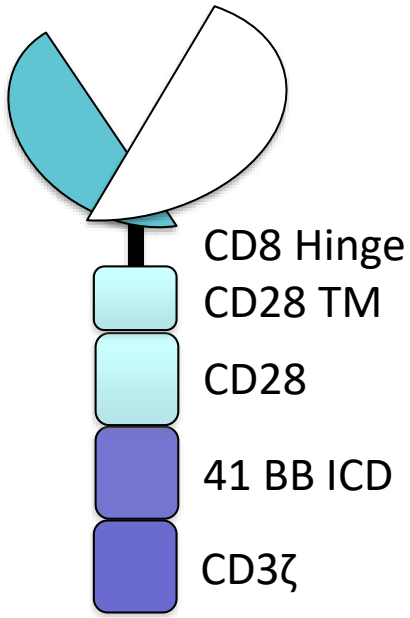
NK Cell-specific CAR Constructs

CARs	Target			Construct (--TM-CD/s-SD)
3rd Gen T-CAR	hMesothelin			scFv-CD28-CD28-CD137-CD3ζ
NK-CAR1v3	hMesothelin			scFv-CD16-2B4-CD3ζ
NK-CAR2v2	hMesothelin			scFv-NKp44-DAP10-CD3ζ
NK-CAR3v2	hMesothelin			scFv-NKp46-2B4-CD3ζ
NK-CAR4v2	hMesothelin			scFv-NKG2D-2B4-CD3ζ
NK-CAR5	hMesothelin			scFv-NKG2D-CD137-CD3ζ
NK-CAR6	hMesothelin			scFv-NKG2D-2B4-DAP12-CD3ζ
NK-CAR7v2	hMesothelin			scFv-NKG2D-2B4-DAP10-CD3ζ
NK-CAR9	hMesothelin			scFv-NKG2D-CD137-2B4-CD3ζ
NK-CAR10	hMesothelin			scFv-NKG2D-CD3ζ

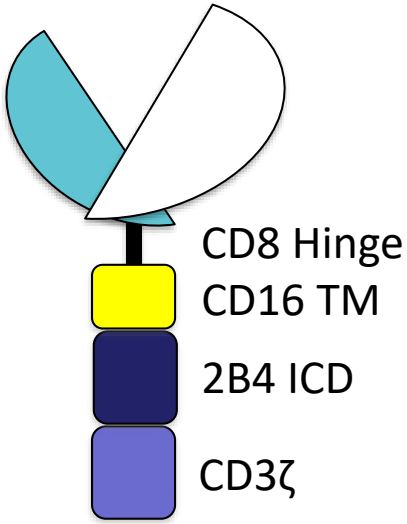
All have CD8 hinge and CD3ζ signaling domain

Fate THERAPEUTICS

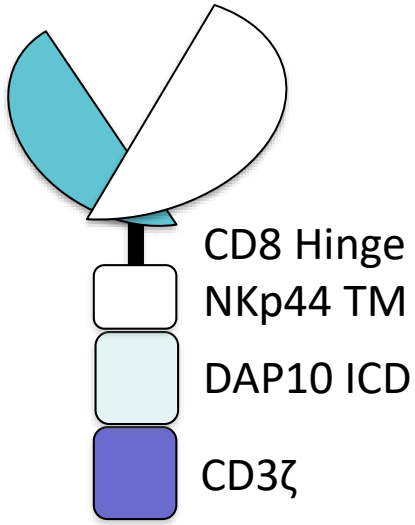
Development of iNK Cell-specific CAR Constructs



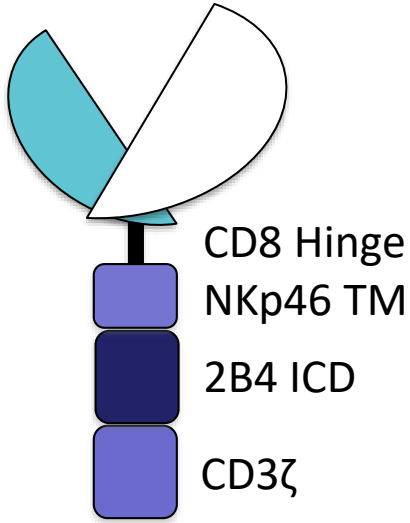
3rd Generation
T Cell CAR



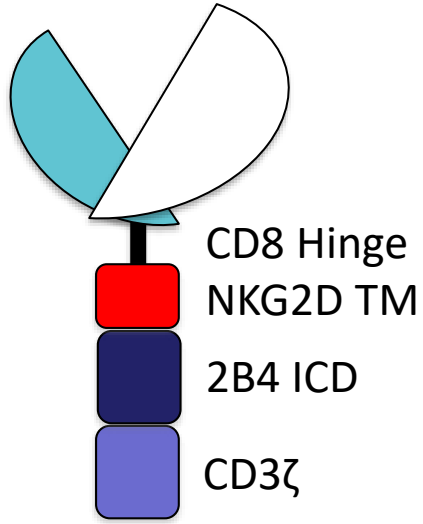
NK CAR 1



NK CAR 2



NK CAR 3



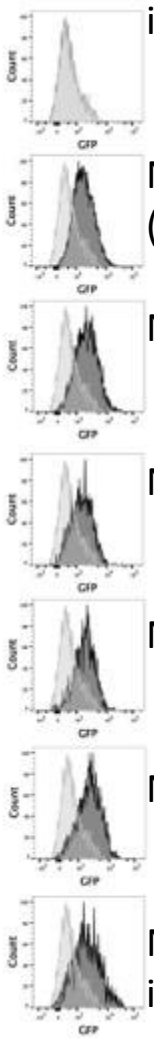
NK CAR 4

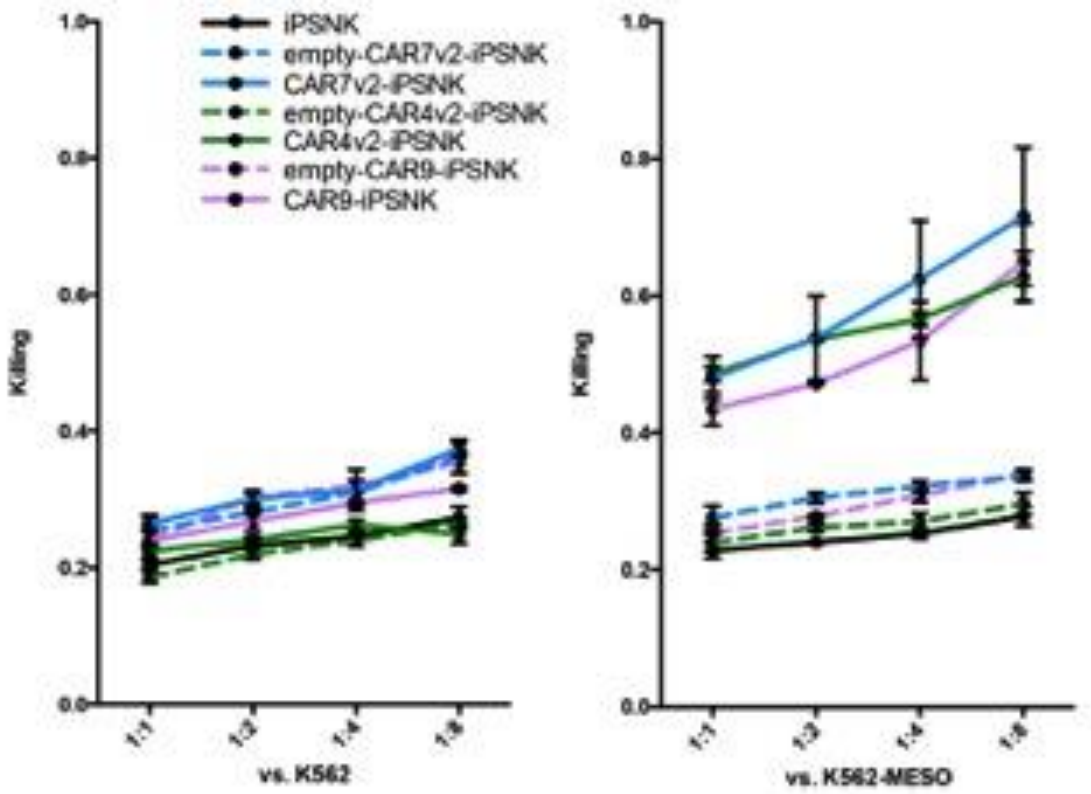
- **Developed a total of 12 unique NK cell-specific CARs**
- **Screened for best activity using NK cells vs mesothelin-expressing tumors**

Fate THERAPEUTICS

Development of iNK Cell-specific CAR Constructs

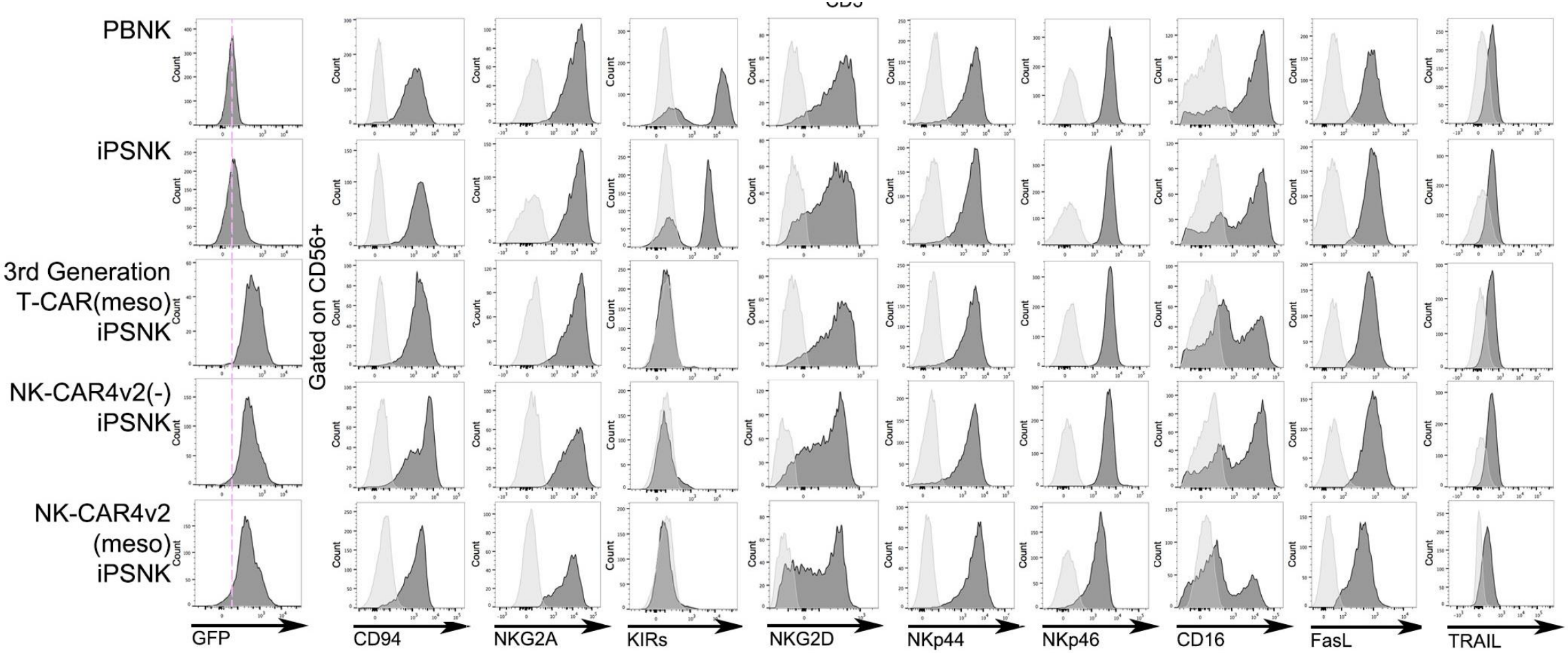
CAR4 Selection for Optimal NK Cell Function





Li, et al. Cell Stem Cell, 2018

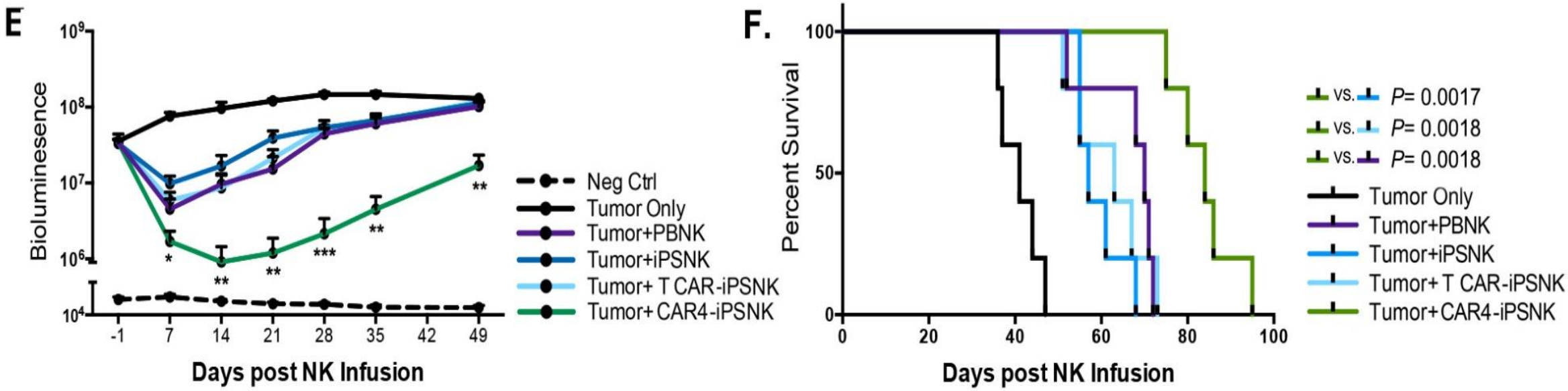
Phenotype of CAR4-expressing iNK Cells



Li, et al. Cell Stem Cell, 2018

CAR4 iNK Cell Function

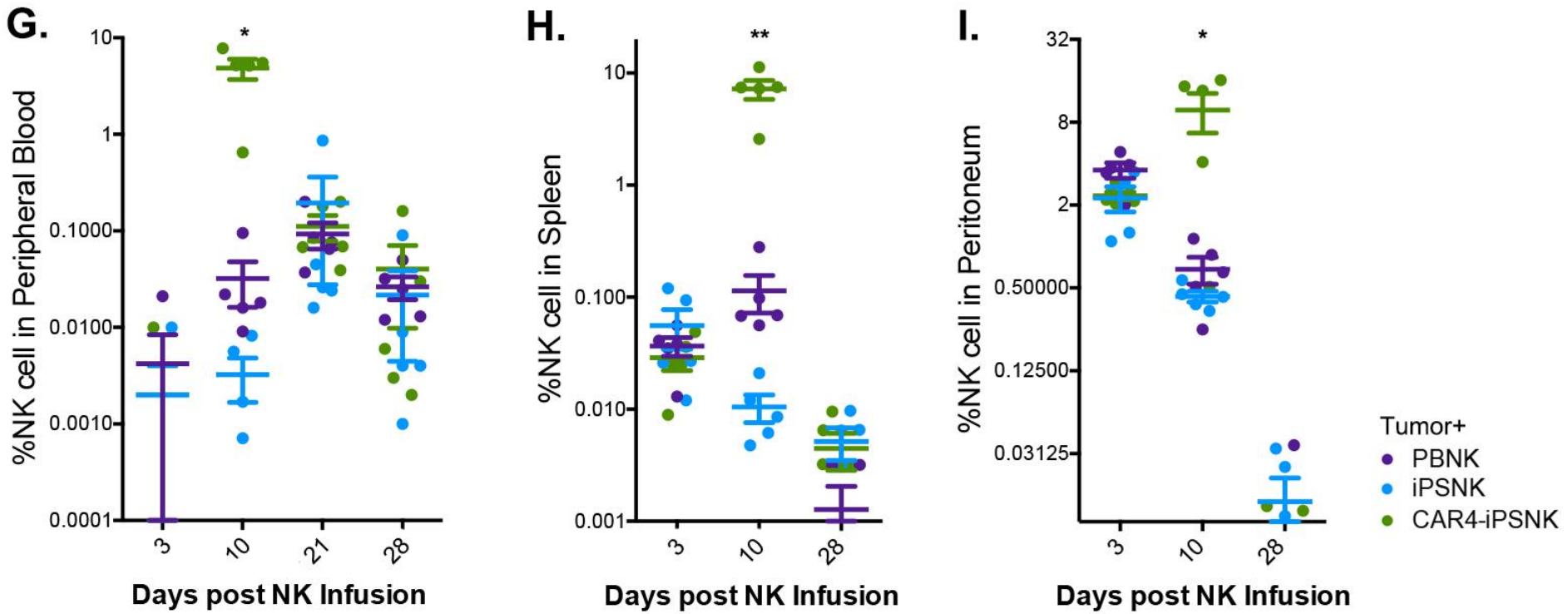
Improved Survival in Ovarian Cancer Model



Li, et al. Cell Stem Cell, 2018

CAR4 iNK Cell Function

In Vivo Expansion upon Target Engagement

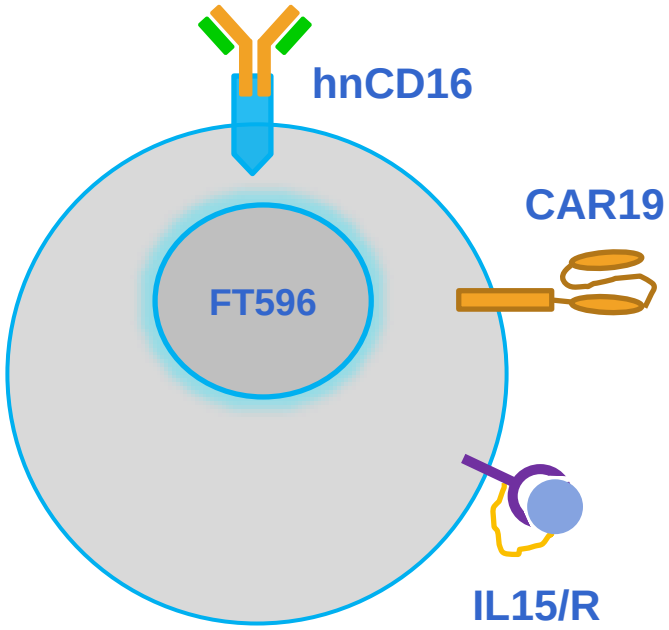


Li, et al. Cell Stem Cell, 2018

FT596: Universal, Off-the-Shelf hnCD16 + CAR19 NK Cell Product

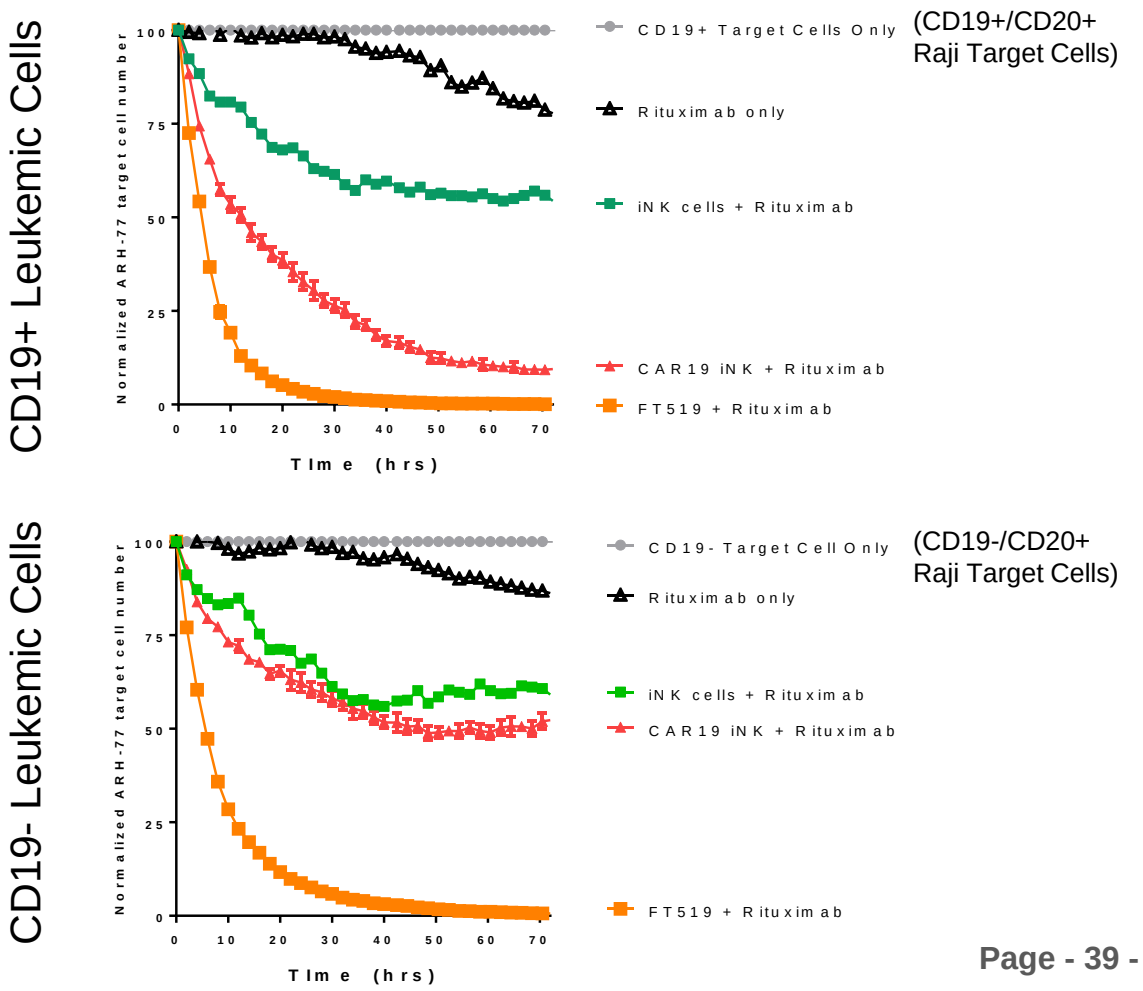
Dual-Targeting for Antigen Escape

Engineered hnCD16 Fc Receptor + CAR19



- ✓ Potent CAR tailor made for NK cell anti-tumor efficacy
- ✓ hnCD16 to multi-node targeting and to mitigate antigen escape
- ✓ IL15/R to enable NK cell persistence without the need for cytokine support

Complementary Mechanisms for Antigen Escape

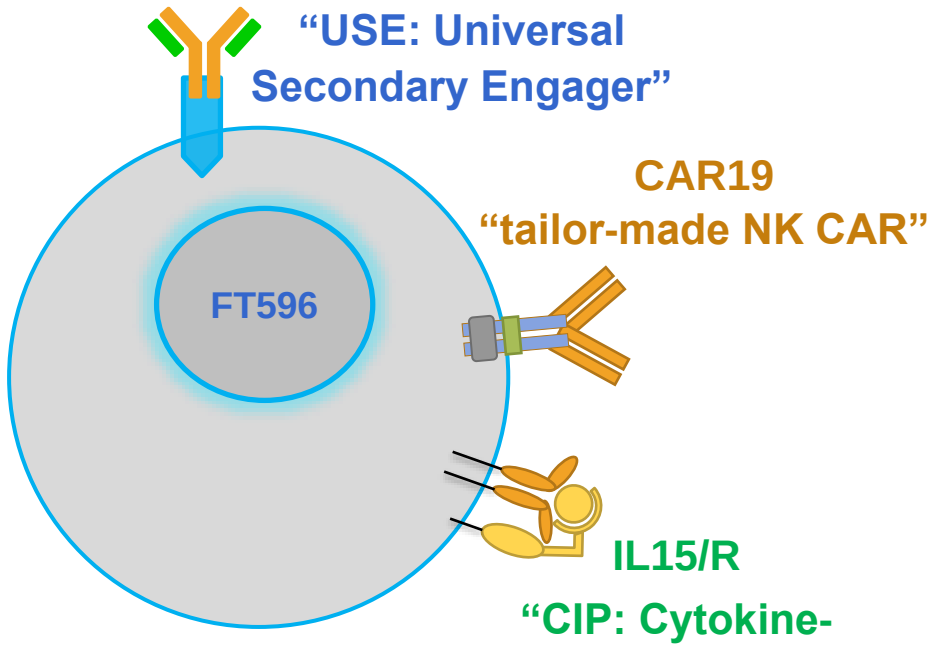


iPSC-derived Cell Product Pipeline

Bob Valamehr, PhD, Chief Development Officer

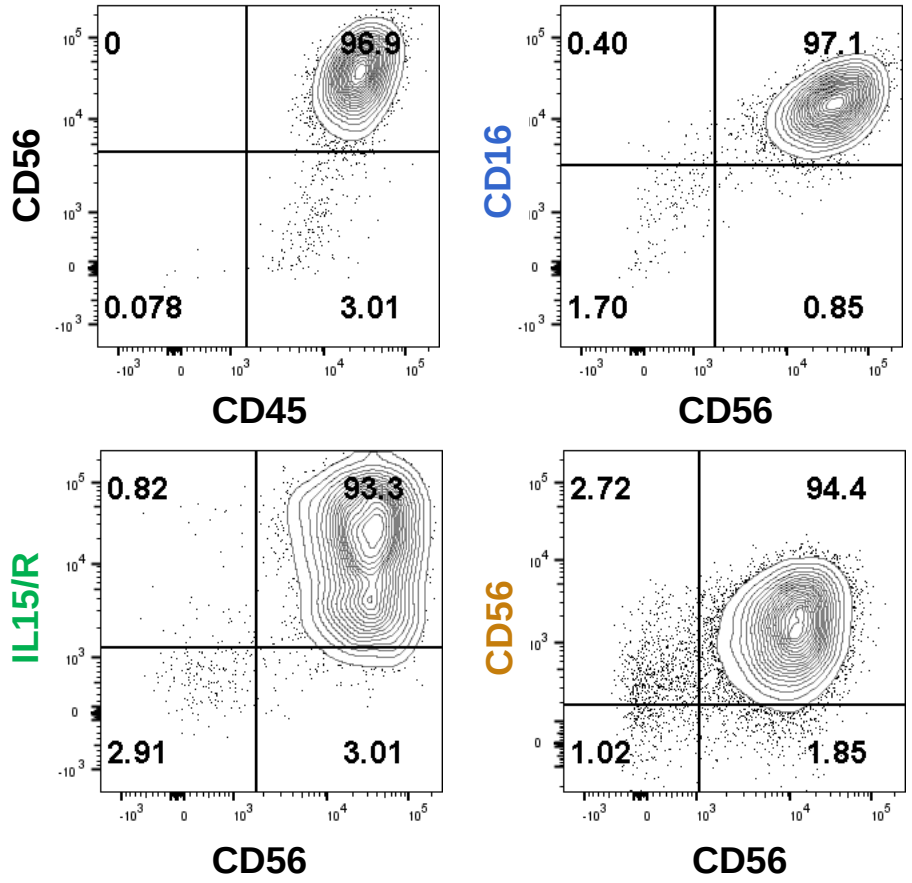
FT596: Universal, Off-the-Shelf hnCD16 + CAR19 NK Cell Product

Multi-modality Engineered Master iPSC Line Cell – CAR | CIP | USE



Planned IND Submission for Mid-2019

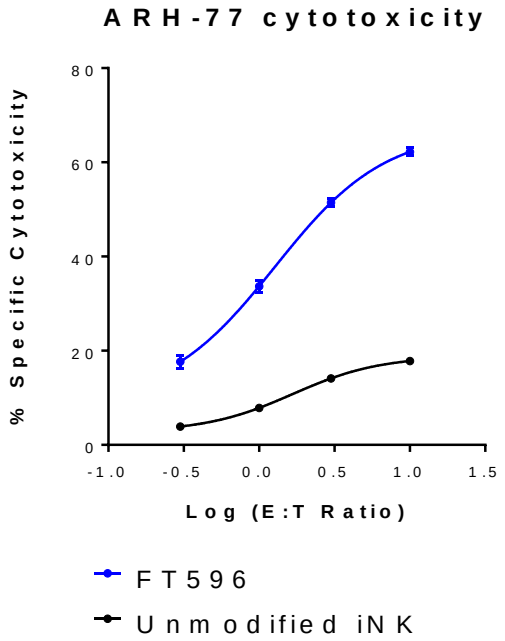
iNK cell Product Profile



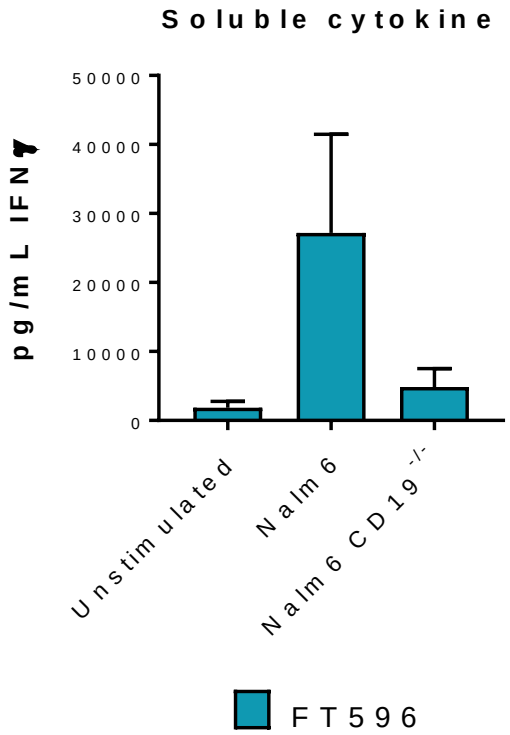
FT596 Cytotoxicity

Enhanced Potency and Specificity

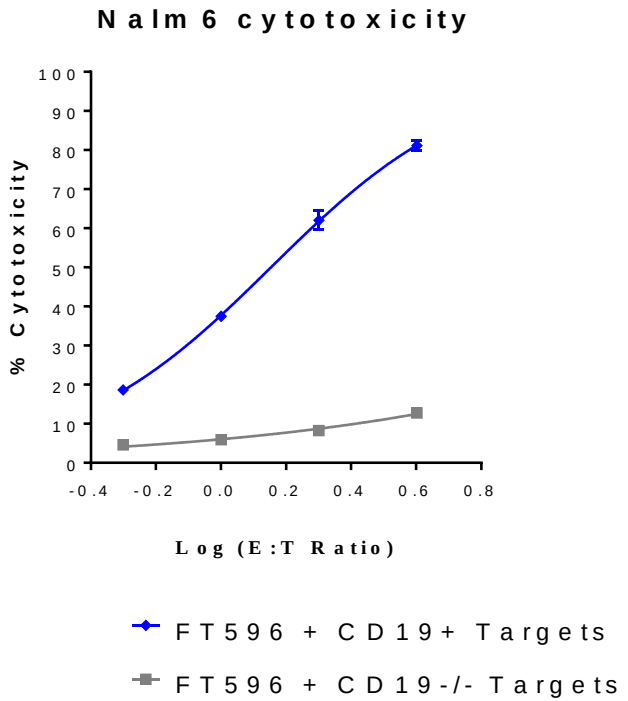
Improve Cytotoxicity Towards CD19+ Target Cells



Enhanced and Specific Cytokine Production



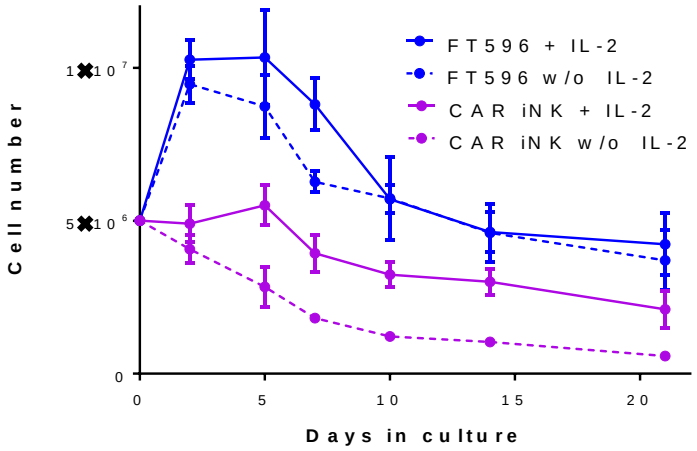
Target Specific Cytotoxicity



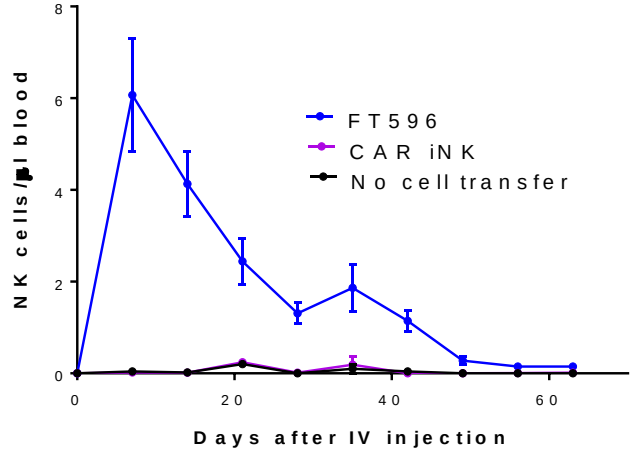
FT596 Persistence

Cytokine-free Persistence and Enhanced In Vivo Expansion

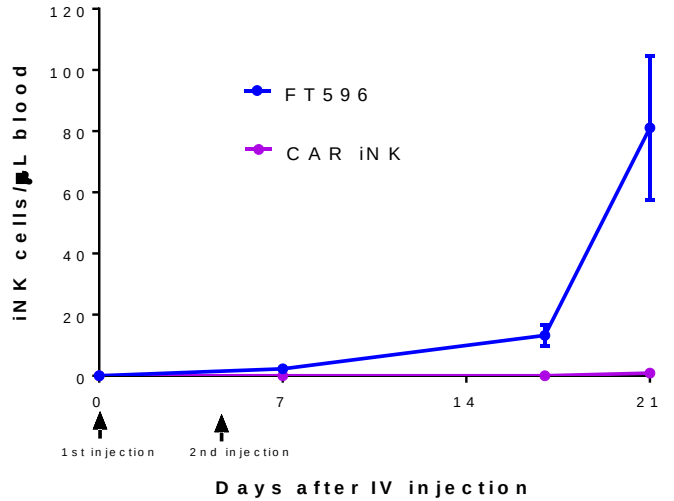
In Vitro Persistence



In Vivo Persistence

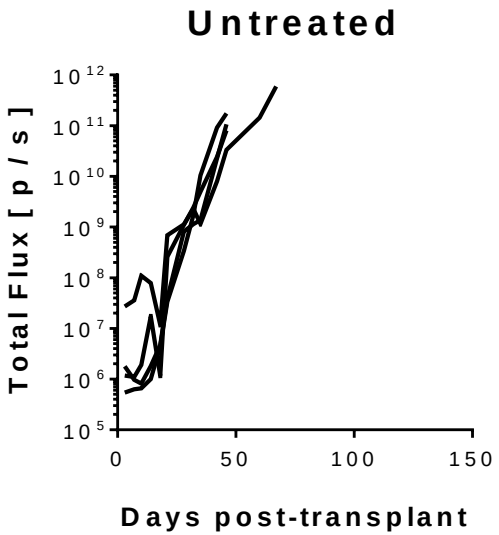


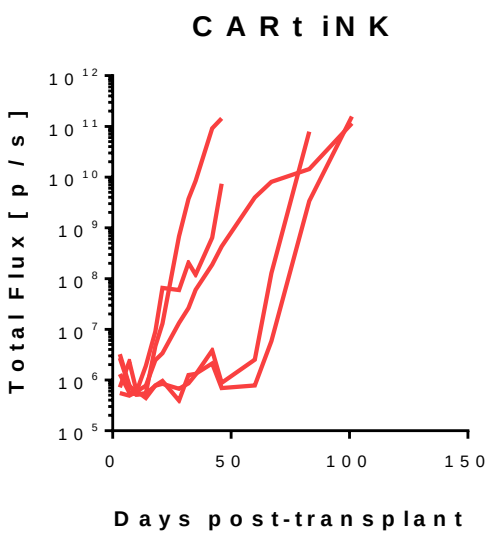
Antigen-driven *In Vivo* Expansion

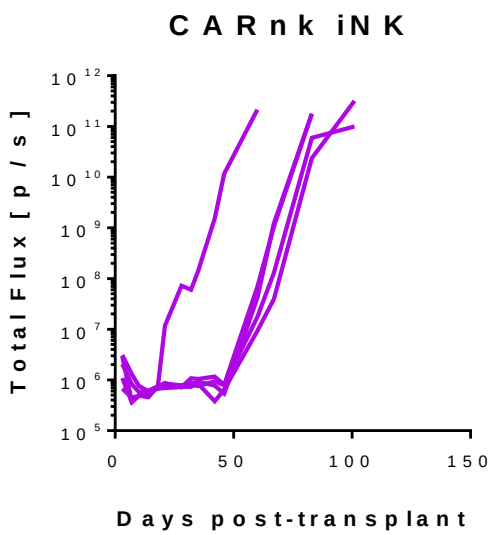


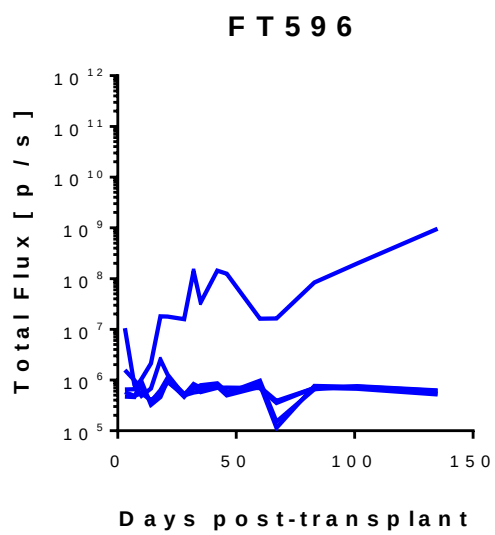
FT596 *In Vivo* Anti-Tumor Activity

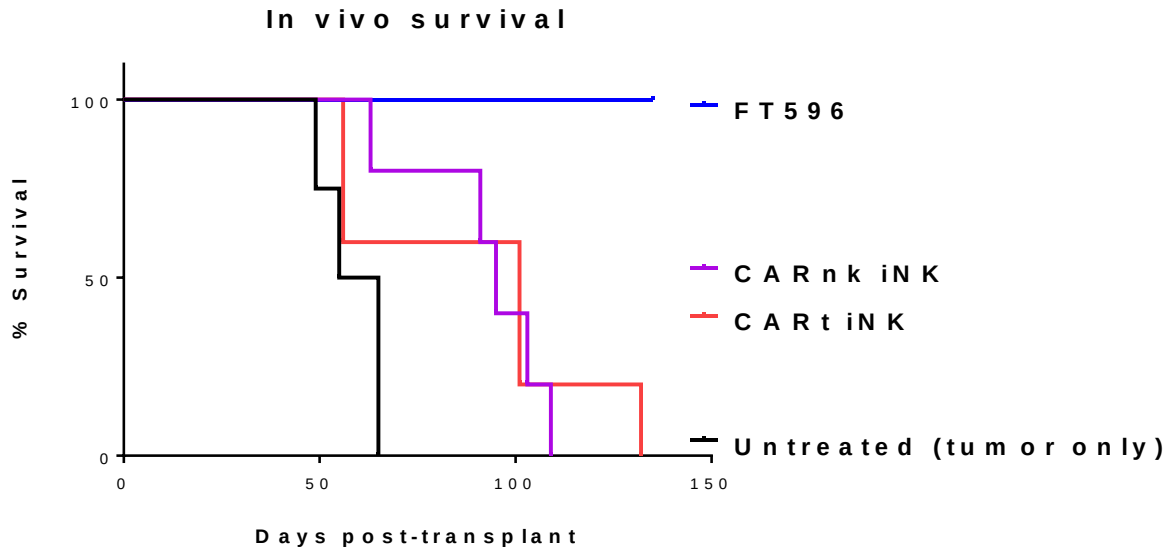
Control of CD19+ Tumor Growth and Long-term Survival





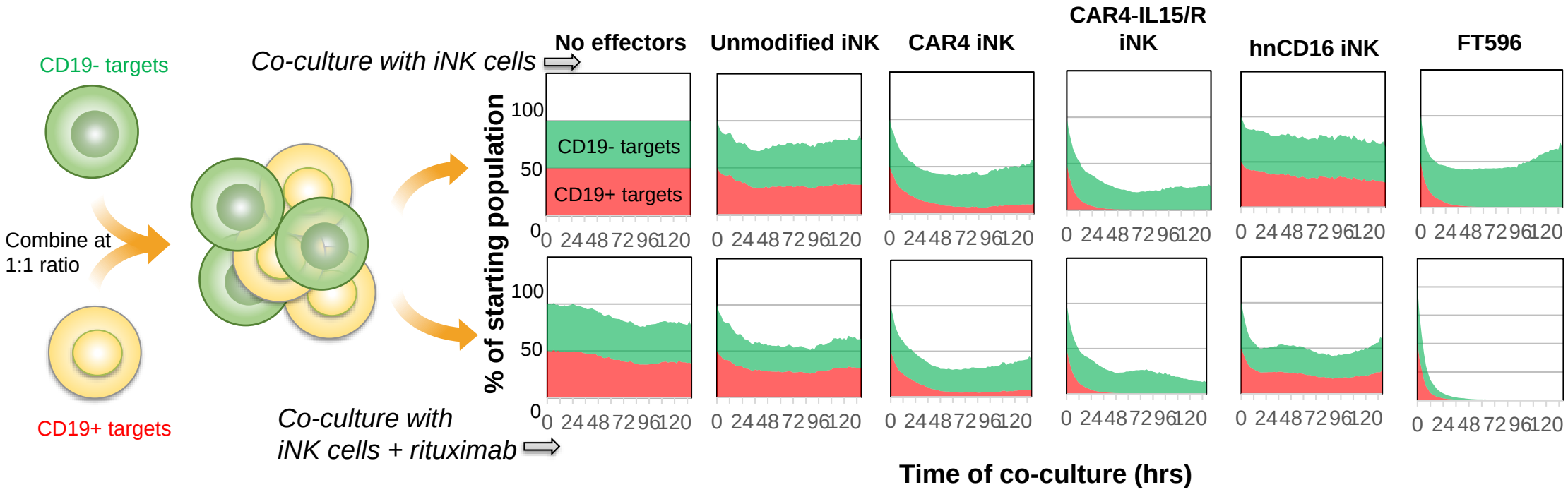




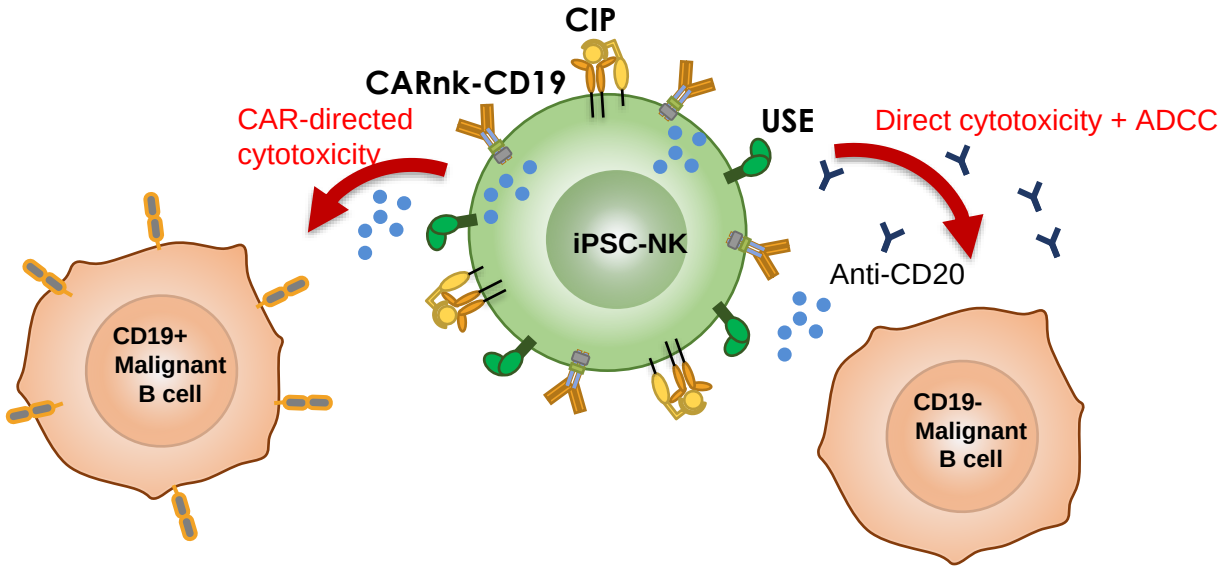


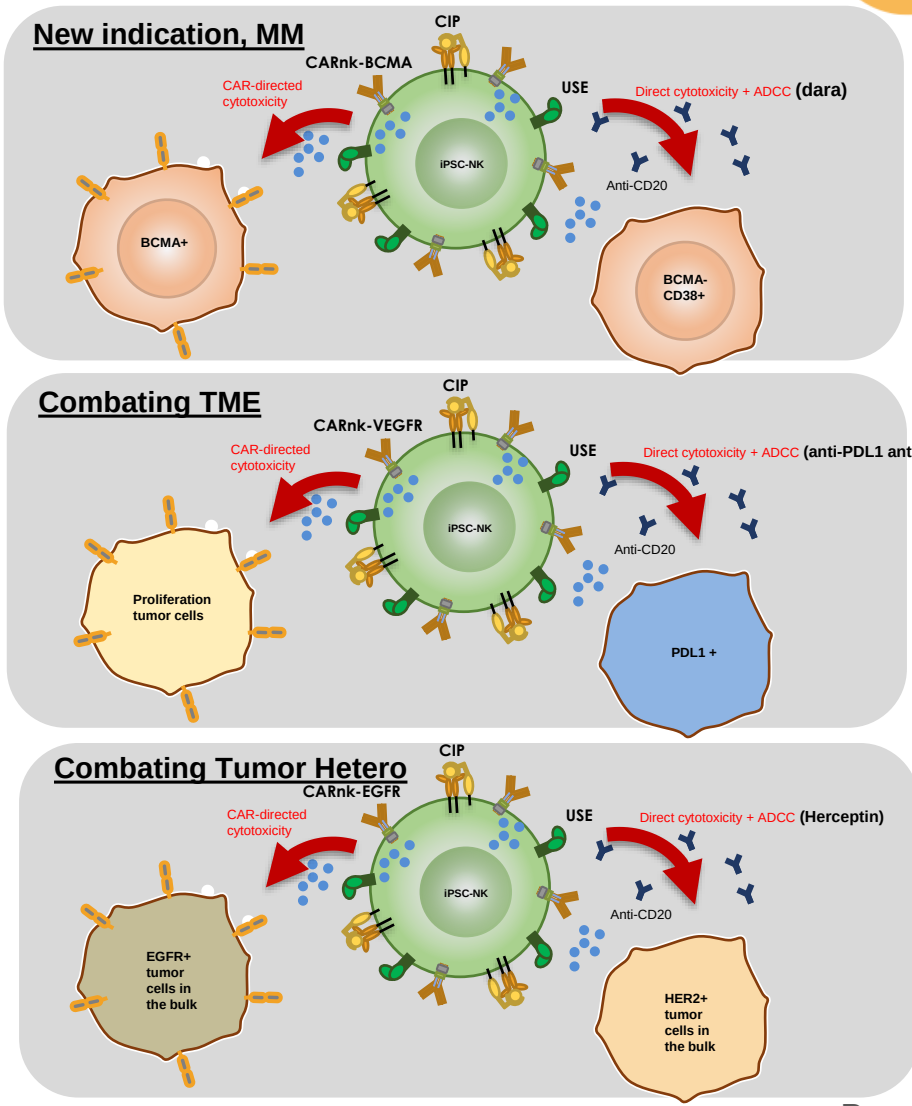
FT596 Mitigation of Antigen Escape

Eradication of CD19+ and CD19- Target Cells in Mixed-culture Cytotoxicity Assay



Versatile iPSC Product Platform: CAR | USE | CIP





Fate THERAPEUTICS

Creating an Off-the-Shelf CART Platform

Michel Sadelain, MD, PhD

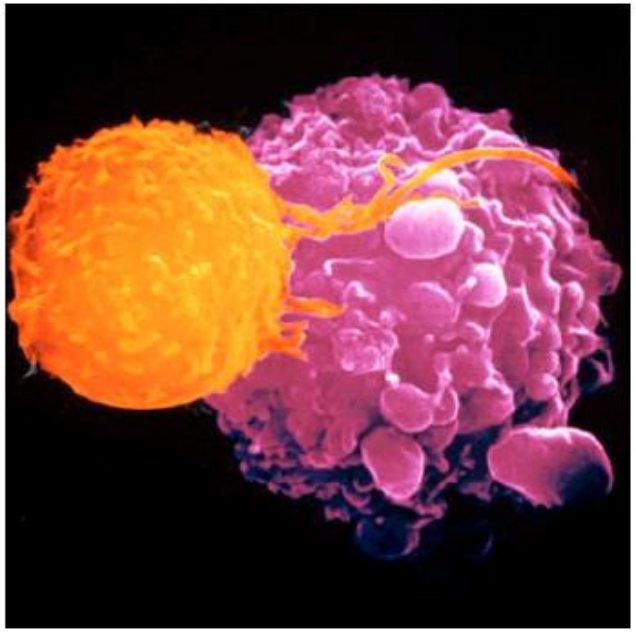
Memorial Sloan Kettering Cancer Center

The Rise of Engineered T Cells as Cancer Drugs

- A major limitation of many current cancer therapeutics is their lack of curative potential.
- Curative immunotherapy must harness T cell specificity, persistence and potency.

- Safety
- Efficacy

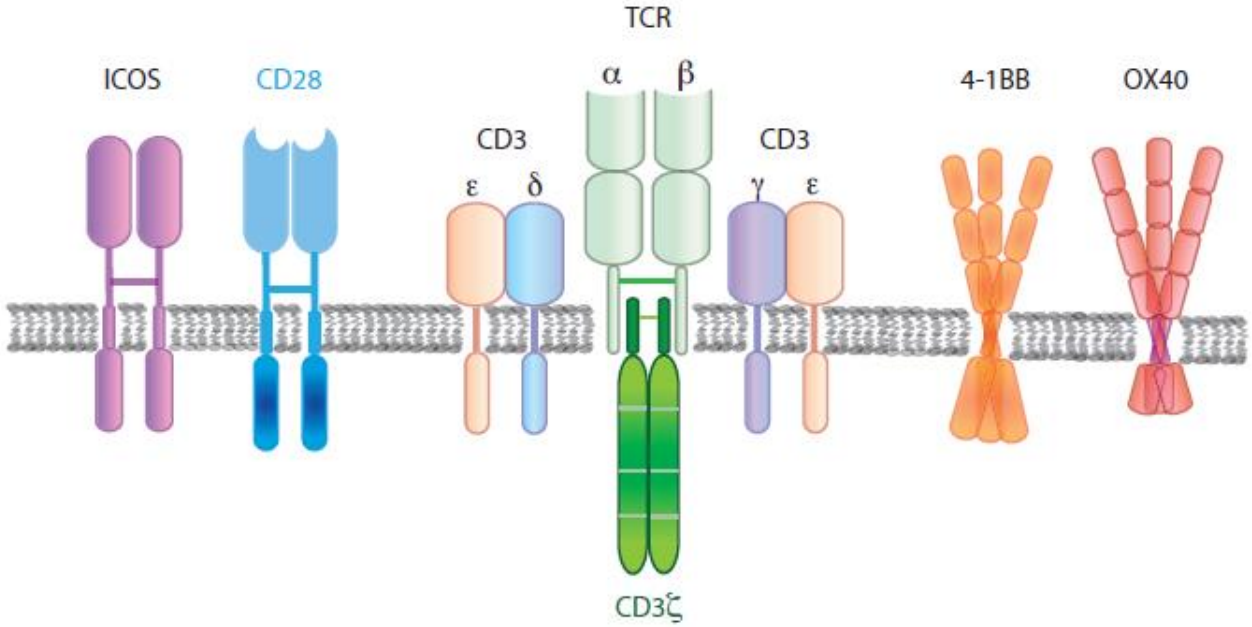
- Specificity
- Long-acting
- Potency



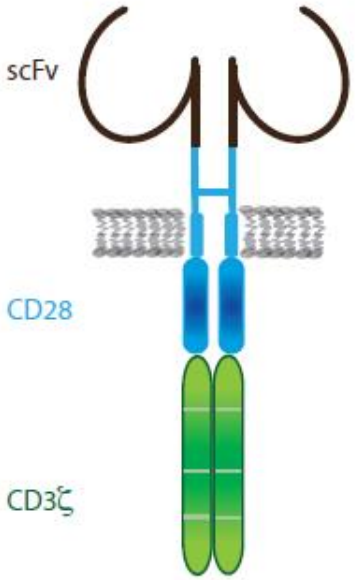
Memorial Sloan Kettering Cancer Center

Physiological and Synthetic Receptors for T Cell Engineering

The TCR/CD3 complex and costimulatory constellation



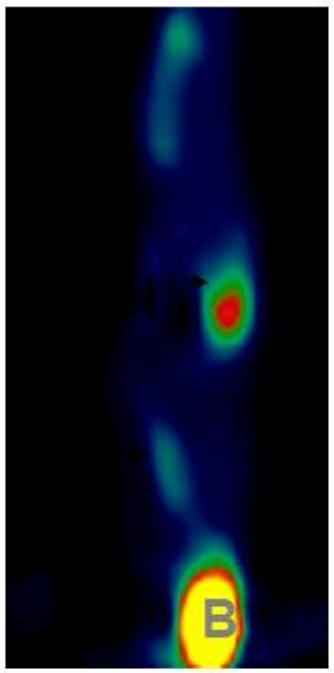
CARs



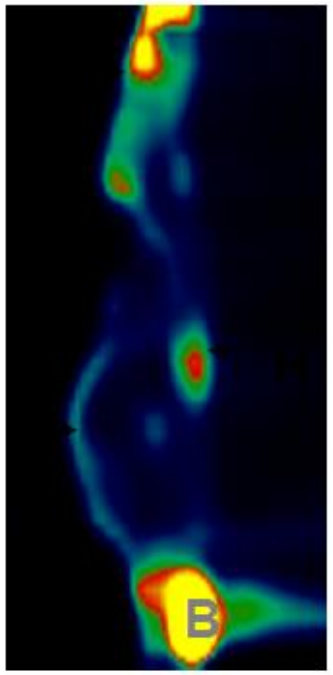
Sadelain, Riviere & Brentjens, *Nat Rev Cancer*, 2003
Sadelain, *AACR Education Program*, 2014

Memorial Sloan Kettering Cancer Center

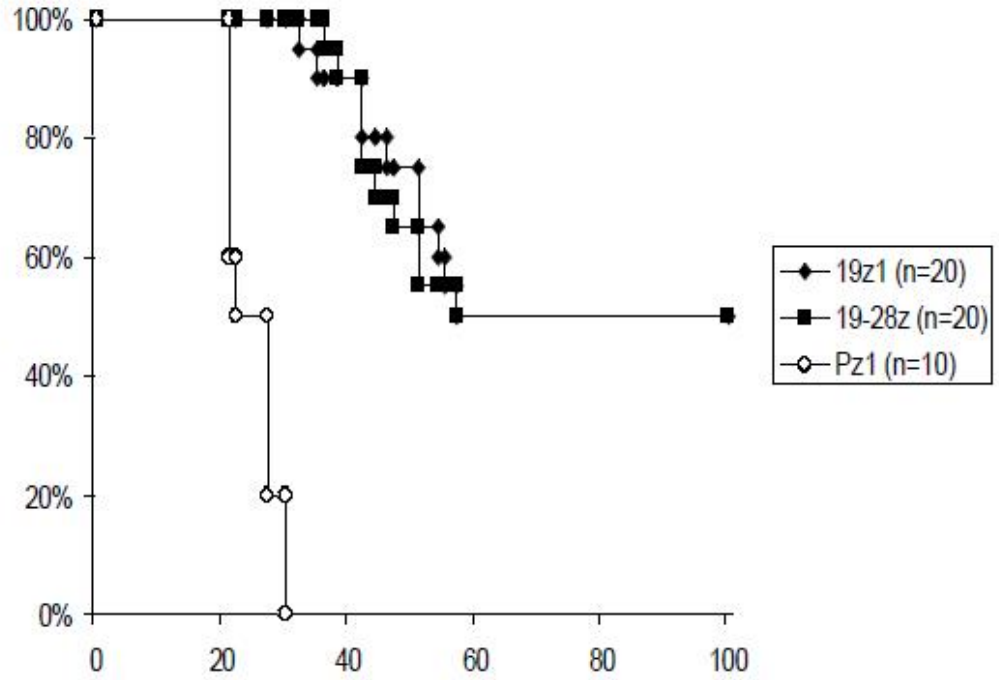
CD19 CAR T Cells Eradicate Systemic B-cell Malignancies in Mice



Tumor Free



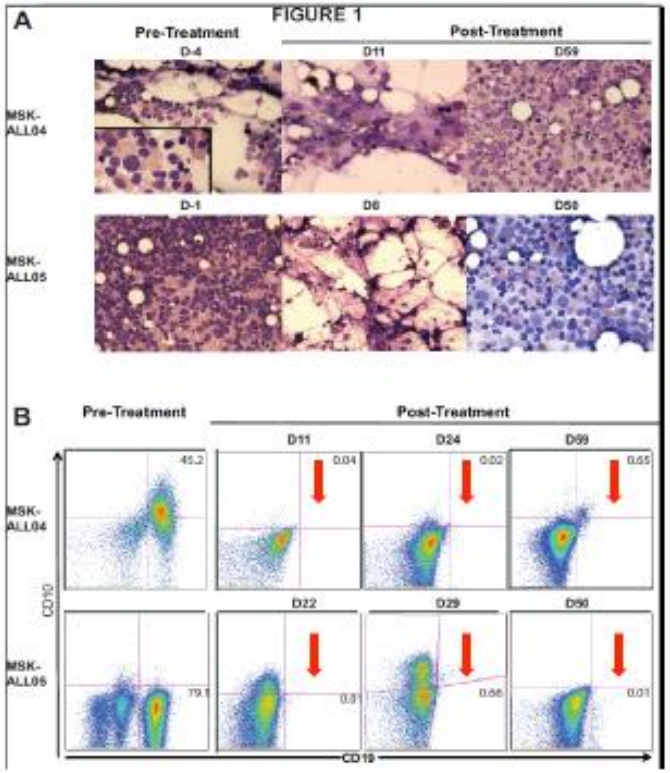
Untreated
4 weeks



Brentjens et al, *Nat Med*, 2003

Memorial Sloan Kettering Cancer Center

Rapid Leukemia Eradication Mediated by 19-28z CAR T Cells



Brentjens, Davila, Rivière *et al*, *Science Transl Med*, March 2013

Science, December 2013

Table 1. Responses to CAR T-Cell Therapy.*

Disease	Response Rate	Comments	Reference
	percent		
Leukemia			
B-cell acute lymphoblastic leukemia (in adults)	83–93	High initial remission rates; unresolved issue is whether CAR T-cell therapy is definitive therapy or should be followed by allogeneic hematopoietic stem-cell therapy	Park et al.,[7] Davila et al.,[8] Turtle et al.[9]
B-cell acute lymphoblastic leukemia (in children)	68–90	Approximately 25% of patients reported to have a relapse with CD19-negative or CD19-low leukemia; CD22 CAR T cells may improve survival among some patients with CD19 relapses	Maude et al.,[10] Maude et al.,[11] Fry et al.,[12] Lee et al.[13]
Chronic lymphocytic leukemia	57–71	Relapse is rare in patients who have a complete response; ibrutinib appears to increase response rates	Porter et al.,[14] Turtle et al.[15]
Lymphoma			
Diffuse large B-cell lymphoma	64–86	Approximately 40–50% of patients reported to have a durable complete response	Turtle et al.,[16] Kochenderfer et al.,[17] Schuster et al.,[18] Neelapu et al.[19]
Follicular lymphoma	71	At a median follow-up of 28.6 mo, the response was maintained in 89% of patients who had a response	Schuster et al.[18]
Transformed follicular lymphoma	78–83	A total of 3 of 3 patients with transformed follicular lymphoma had a complete response	Turtle et al.,[16] Schuster et al.,[18] Neelapu et al.[19]
Refractory multiple myeloma	25–100	B-cell maturation antigen CAR T cells; stringent complete response in approximately 25% of patients	Ali et al.,[20] Fan et al.,[21] Berdeja et al.[22]
Solid tumors			
Glioblastoma	ND	In case report from phase 2 study, complete response on magnetic resonance imaging after intravenous and cerebrospinal fluid administration of CAR T cells; complete response lasted 7.5 mo	Brown et al.[23]
Pancreatic ductal adenocarcinoma	17	In one patient with liver metastasis, CAR T-cell treatment produced a complete metabolic response in the liver but was ineffective against the primary pancreatic tumor	Beatty et al.[24]

* ND denotes not determined.

June and Sadelain, *N Engl J Med*, 2018

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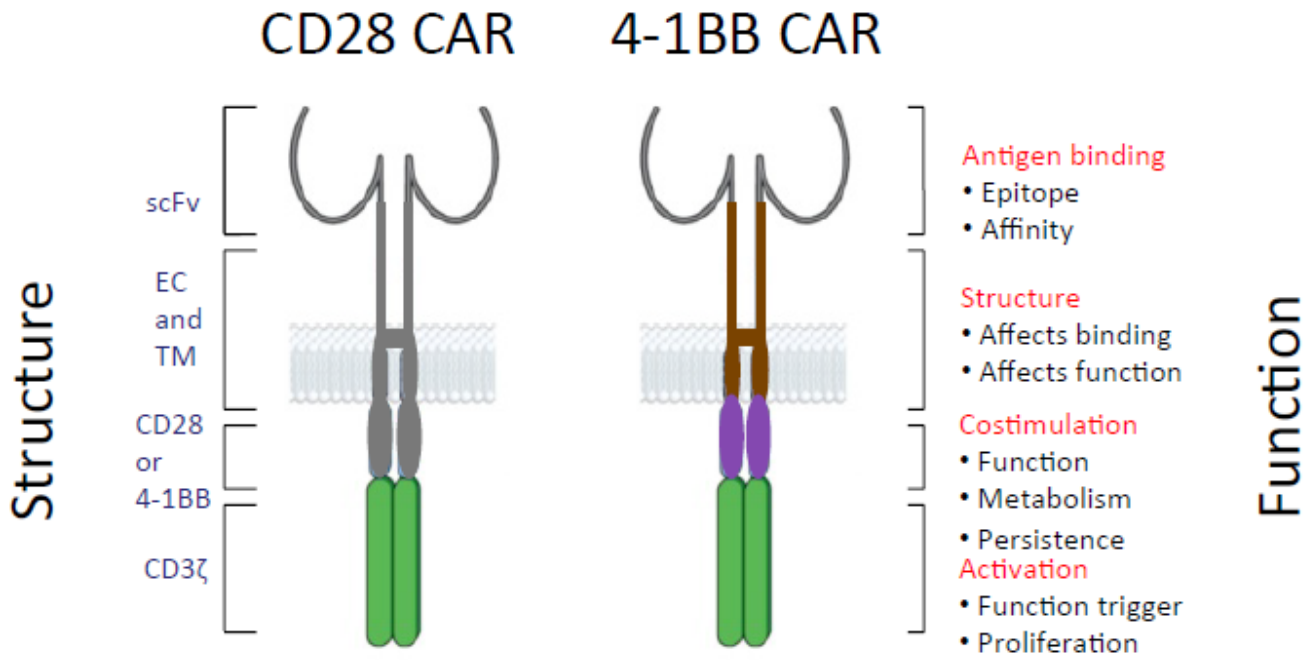
Prototypic CD19 CARs



FDA approved in 2017

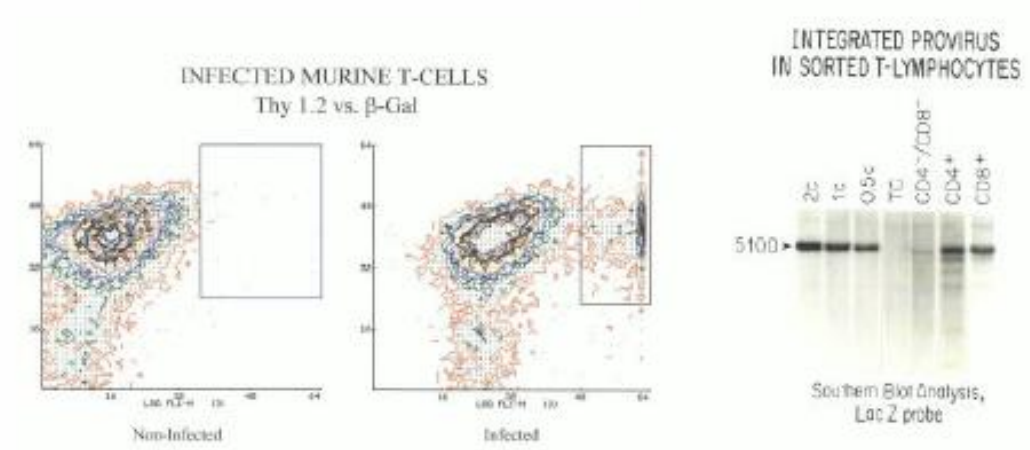
Axicabtagene Ciloleucel	Tisagenlecleucel
(Yescarta)	(Kymriah)

Memorial Sloan Kettering Cancer Center

New Directions in CAR T Cell Engineering

- Exhaustion (i) – Genetic control
- Exhaustion (ii) – Signaling control
- Off-the-shelf – T-iPS CAR T cells

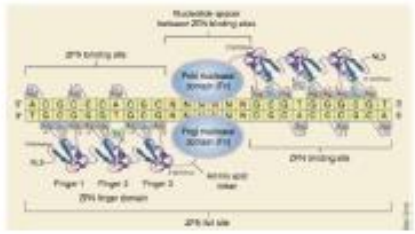
Genetic Engineering Evolution



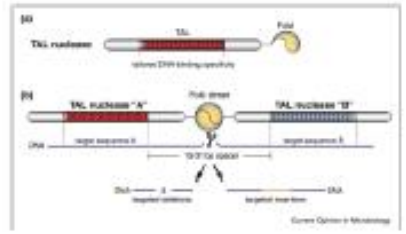
Sadelain and Mulligan, *ICI*, 1992

- Retroviral vectors (gRV, LV)
- Transposons (*Sleeping Beauty*)

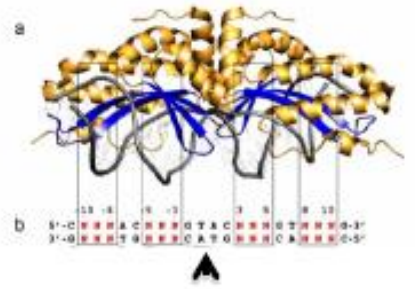
Zinc-finger nuclease (ZFN)



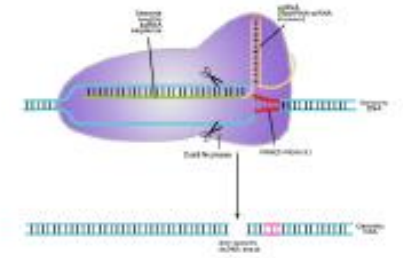
TALE nuclease (TALEN)



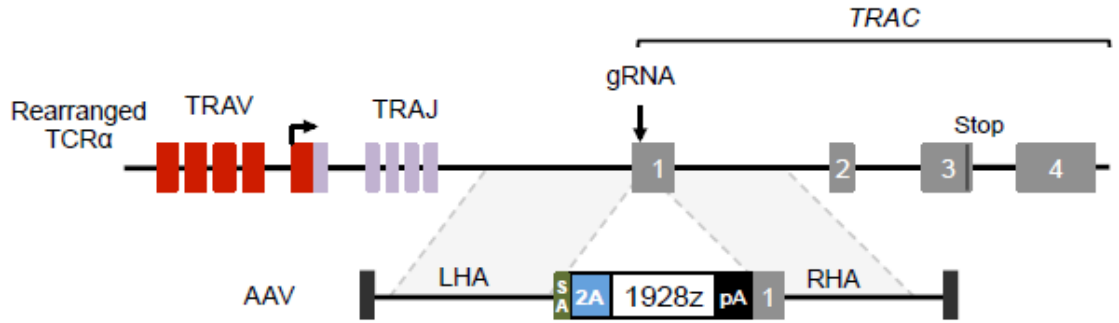
Meganuclease

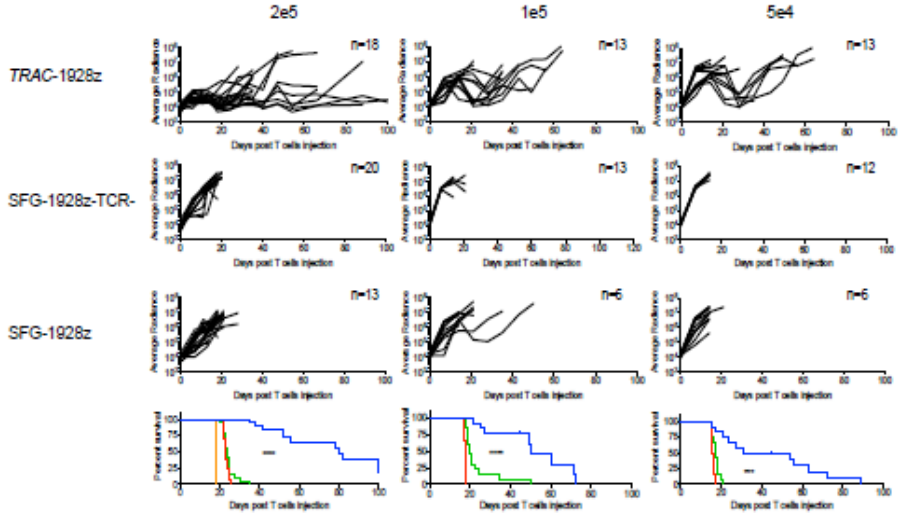


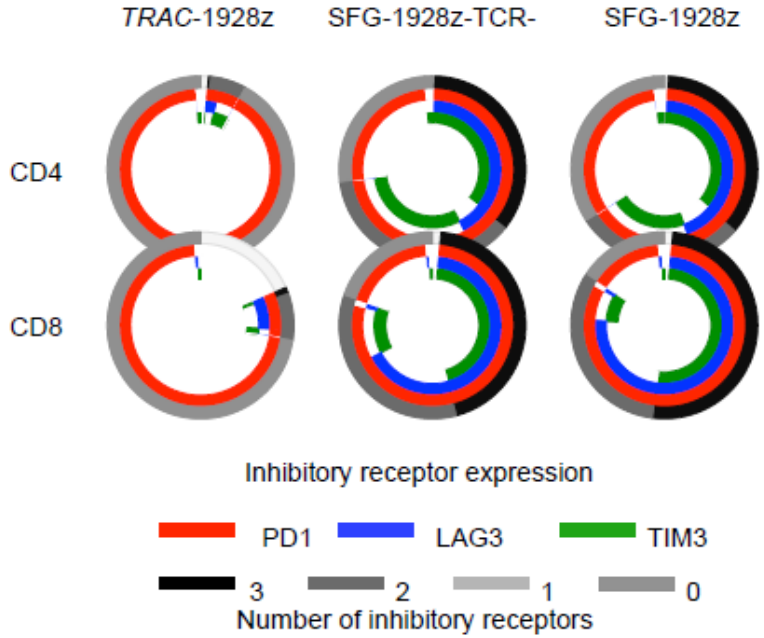
CRISPR-Cas9



CRISPR/Cas9-targeted CAR cDNA Integration into the TRAC Locus



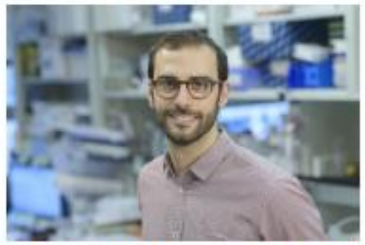




J. Eyquem, J. Mansilla-Soto *et al*, *Nature*, 2017

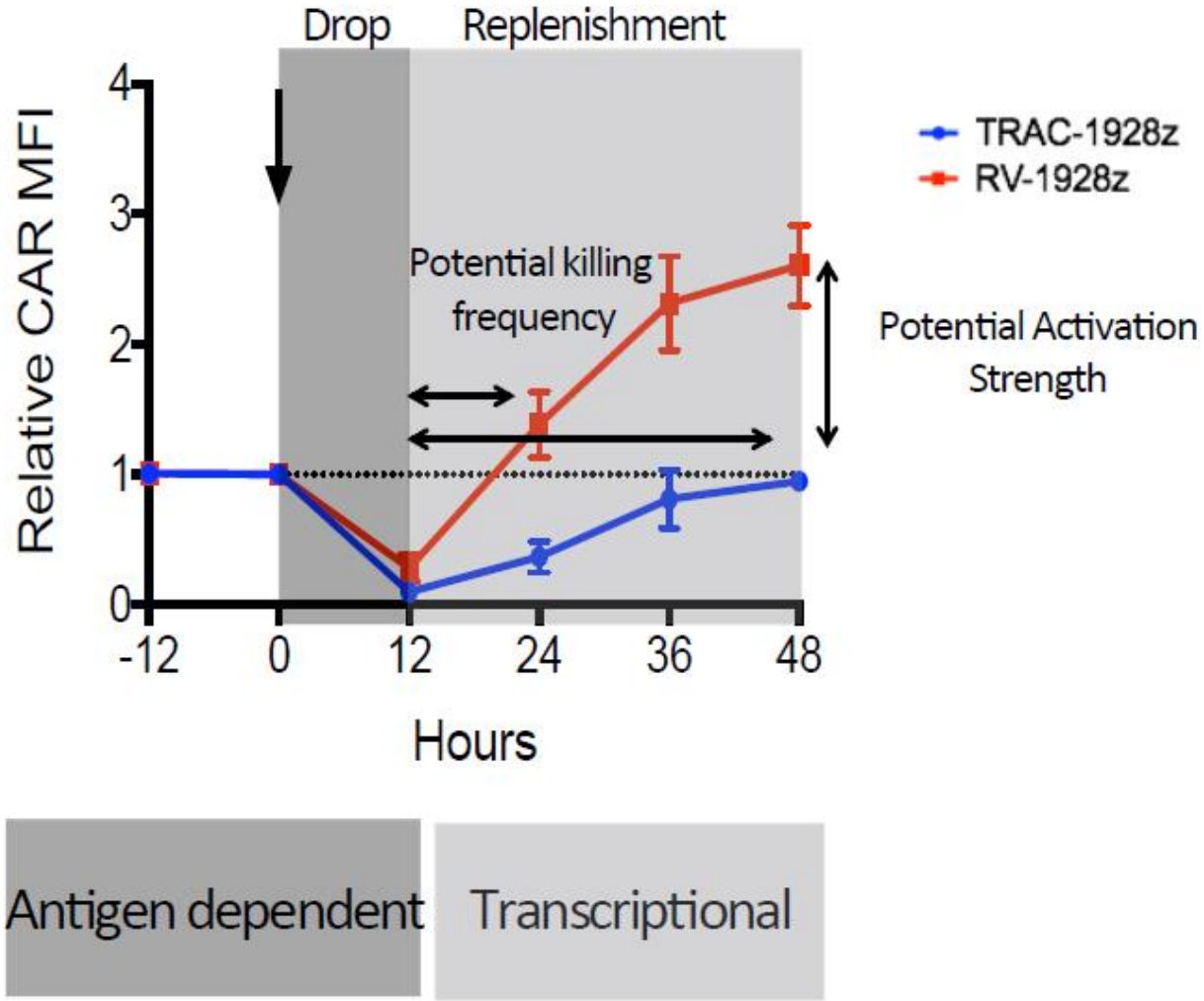
Memorial Sloan Kettering Cancer Center

TRAC-CAR – The Model



Justin Eyquem, PhD

J. Mansilla-Soto, PhD



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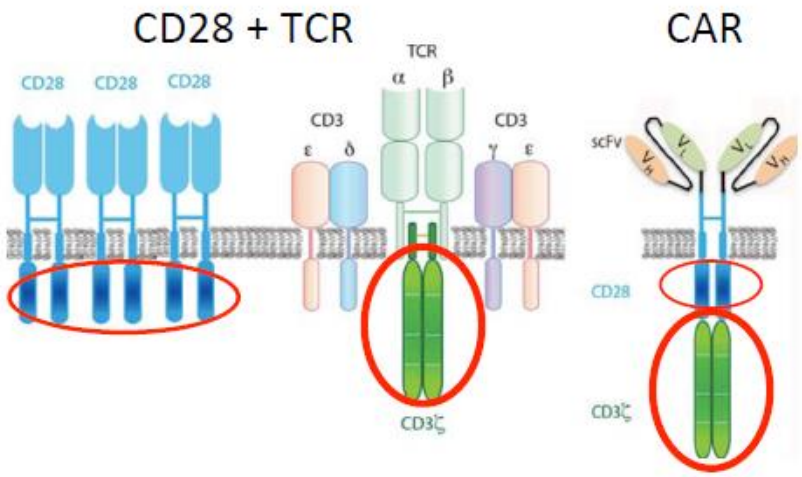
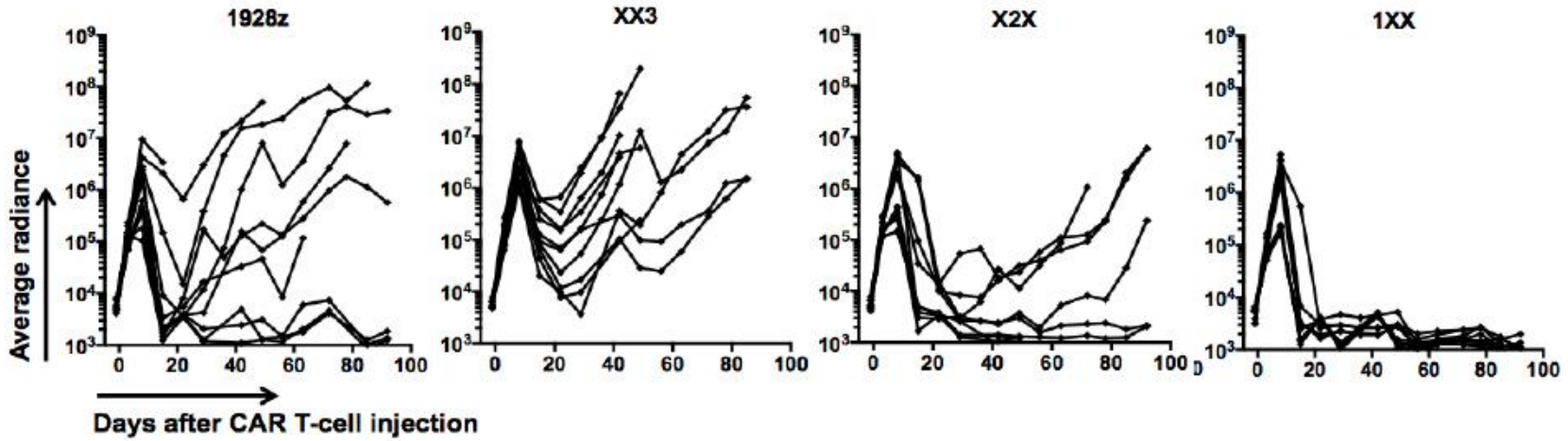
ITAM-based Calibration of Activation Strength in CD28/CD3ζ CARs

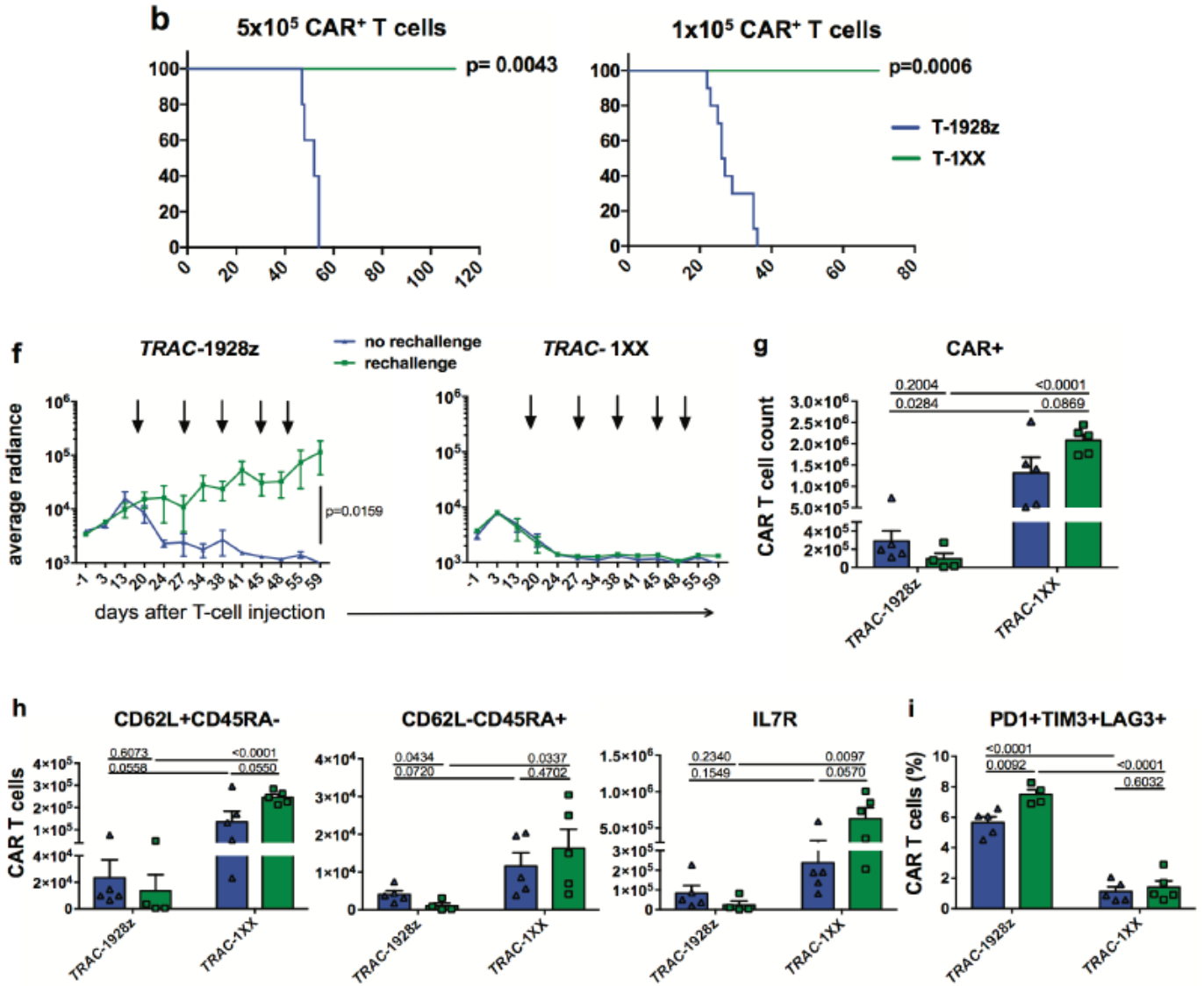




Judith Feucht, Sun Jie, unpublished

TRAC-1XX CAR T Cells

Promote Memory and Protect against Tumor Re-challenge



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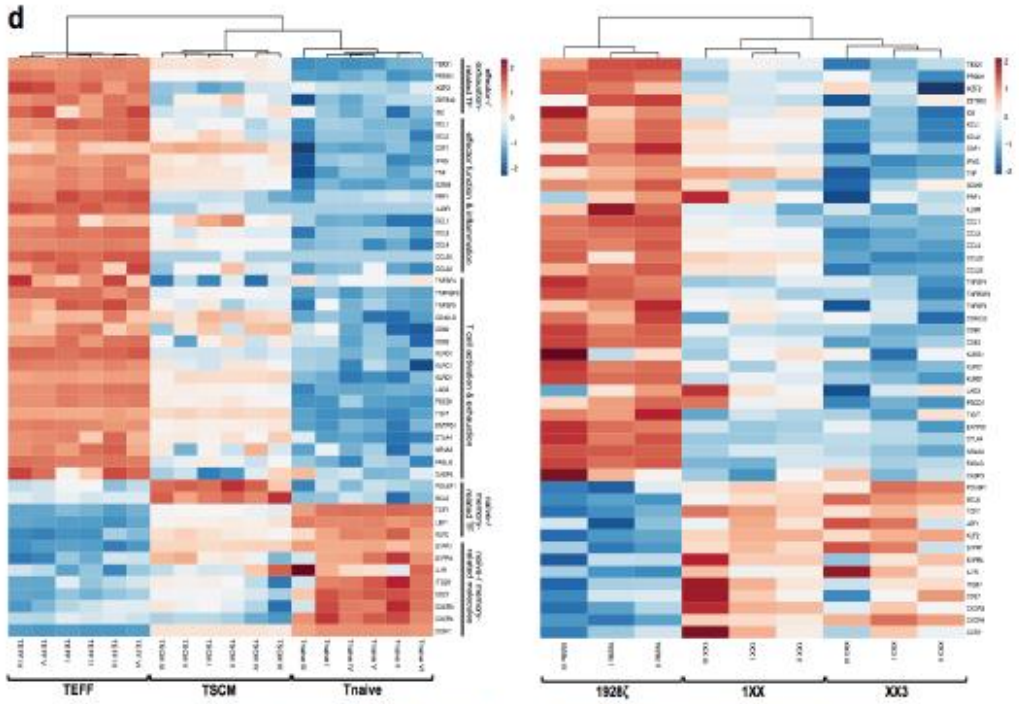
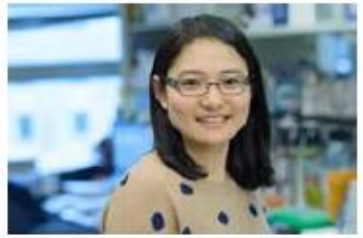
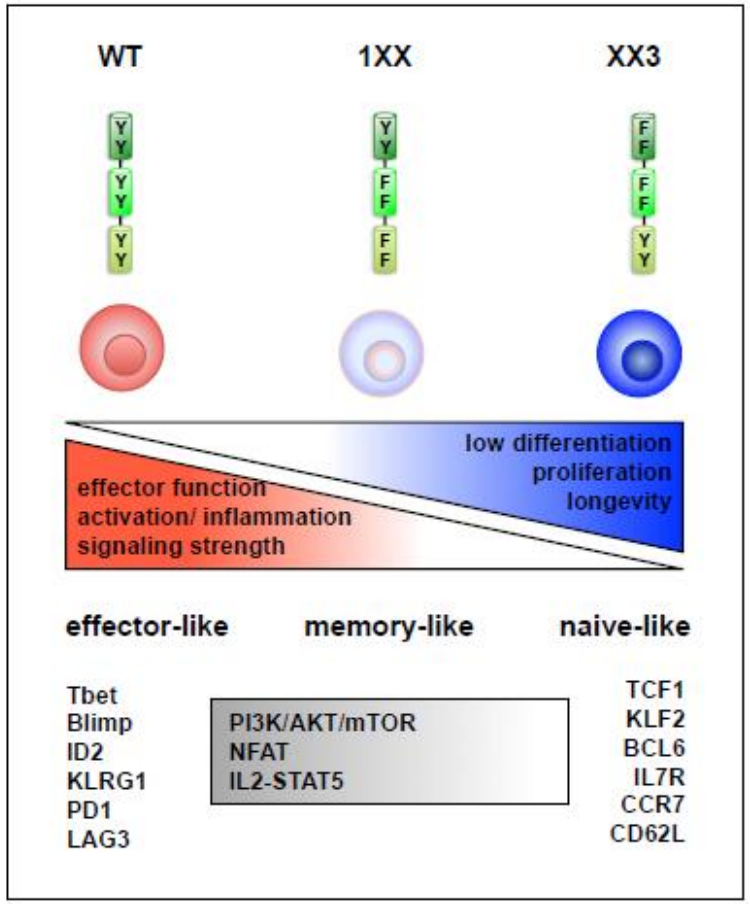
CAR ITAM-calibration Directs T-cell Fate



Judith Feucht, MD



Sun Jie, PhD



J Feucht, S Jie, et al, unpublished

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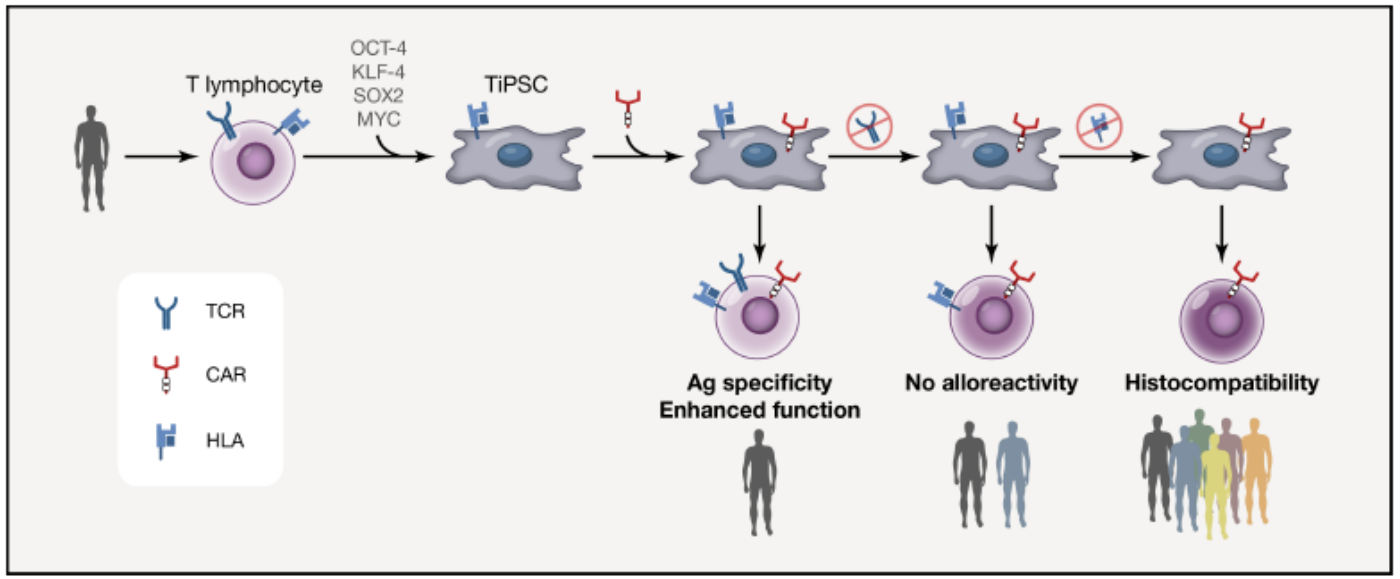
Alternative T-cell Sources

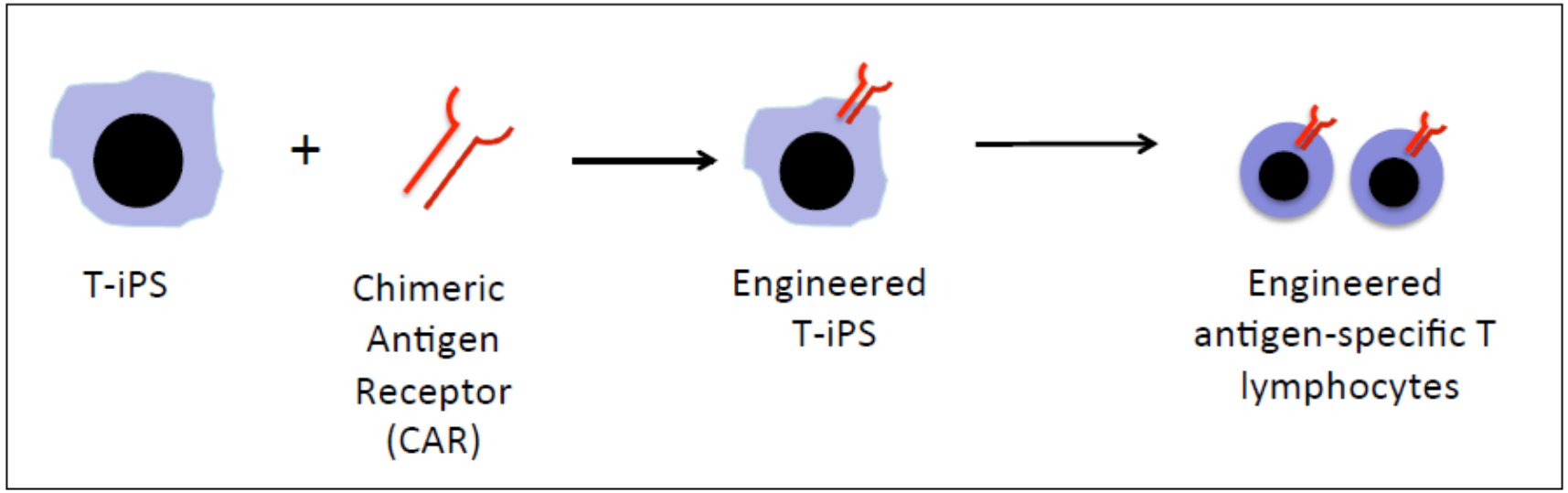
- Autologous T cells
  - Bulk PBMCs
  - T cell subsets
- Allogeneic T cells
  - DLI
  - DLI-TCR$^{-/-}$
  - VSTs
- In vitro generated T cells
  - CB
  - ESC
  - TiPS

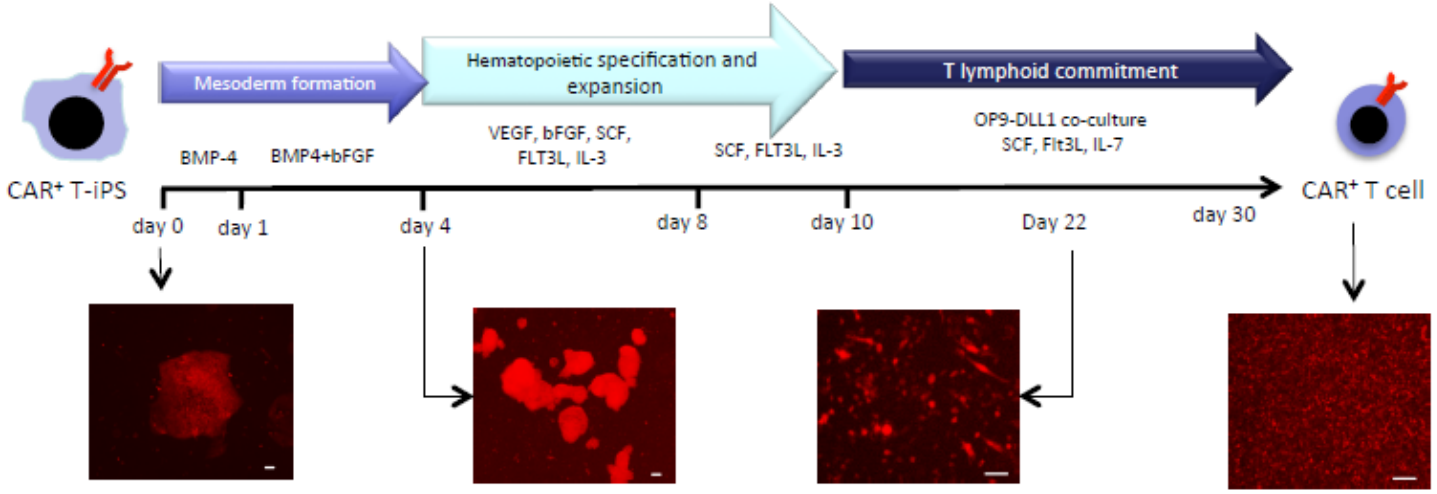


Themeli, Riviere & Sadelain, *Cell Stem Cells*, 2015

Memorial Sloan Kettering Cancer Center

T-iPSC-derived CAR-targeted T Cells





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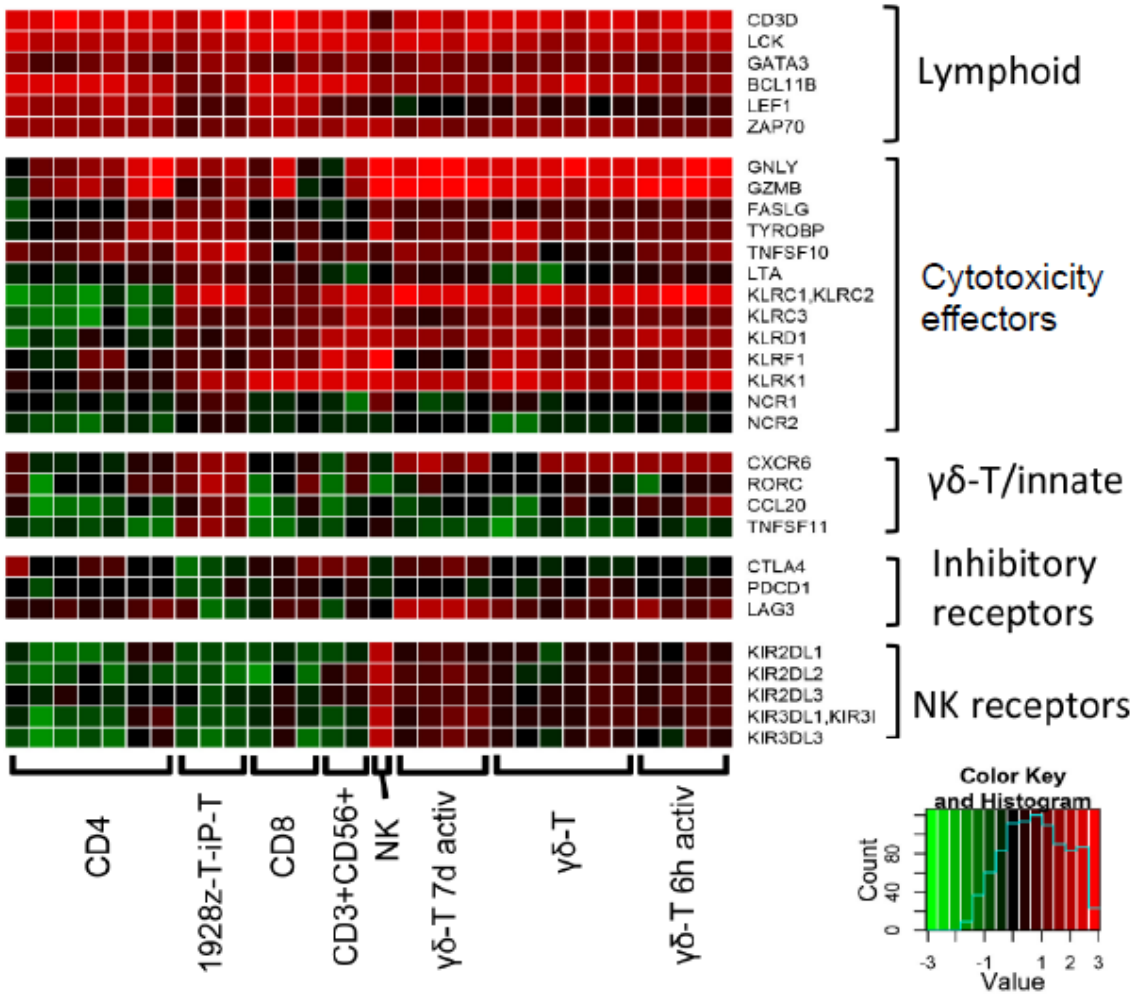
1928z-T-iPSC-derived T Cells Have an Innate-like Phenotype

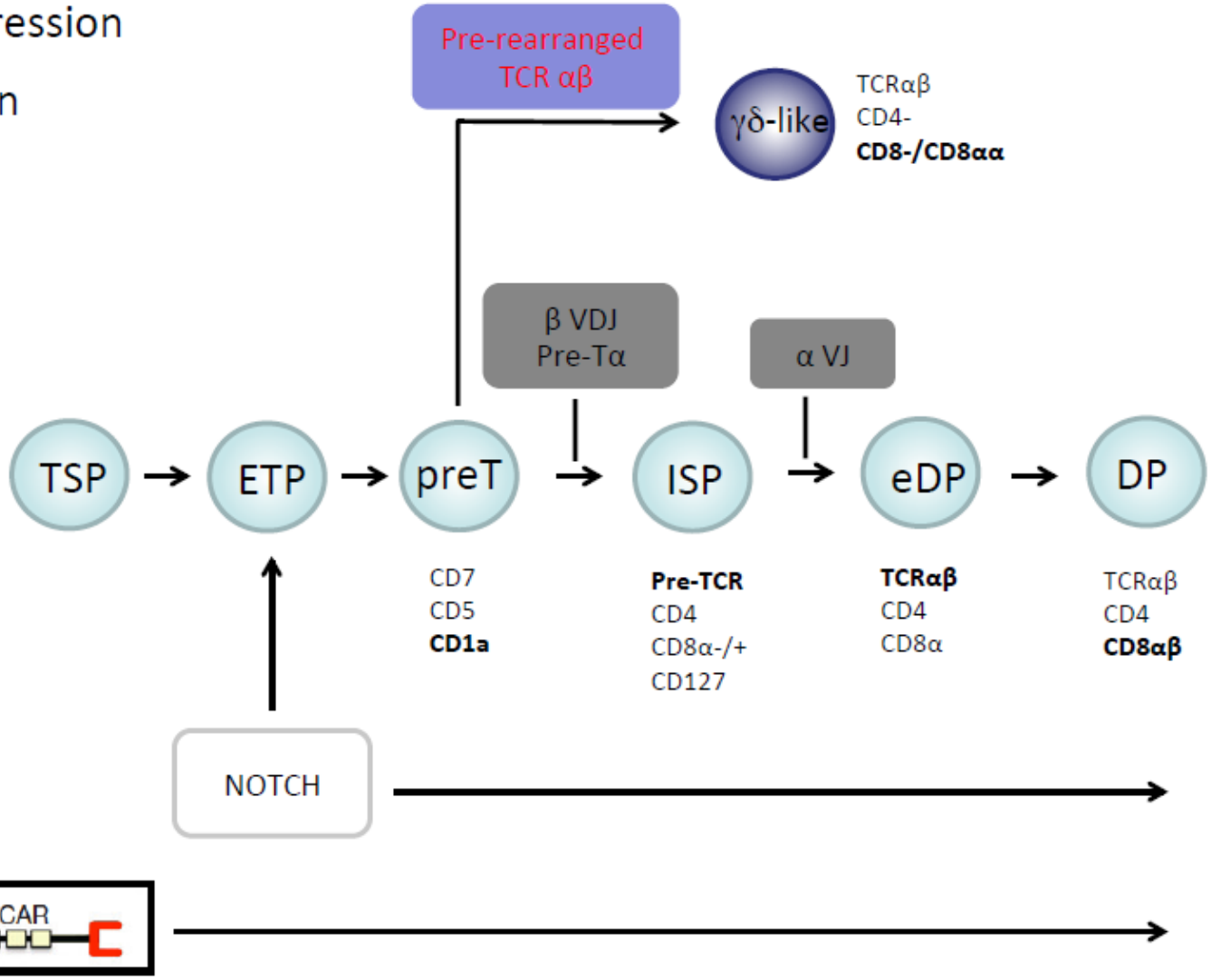


Themeli et al, *Nat Biotechnol*, 2013

T-iPSC Differentiation in the Presence of Re-arranged TCR and CAR

1. Early TCRαβ expression
2. Notch stimulation
3. CAR expression

Sjoukje van der Stegen



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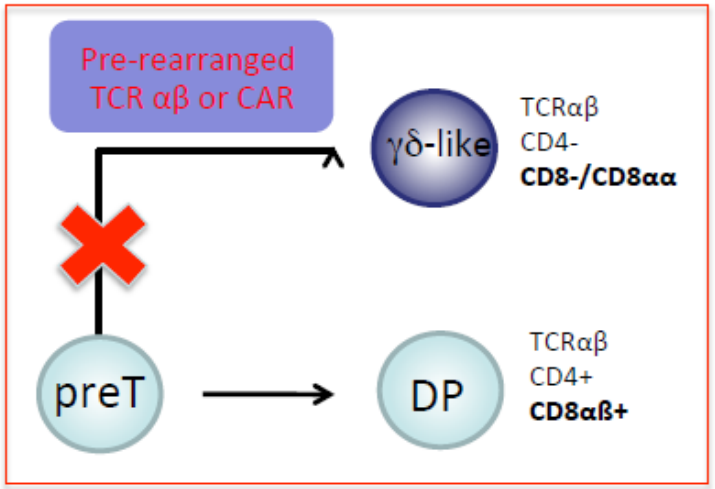
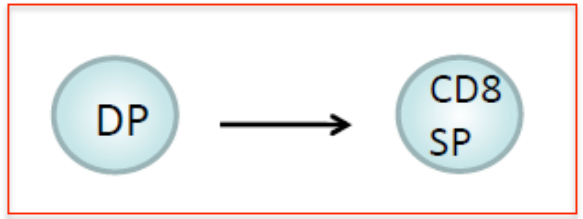
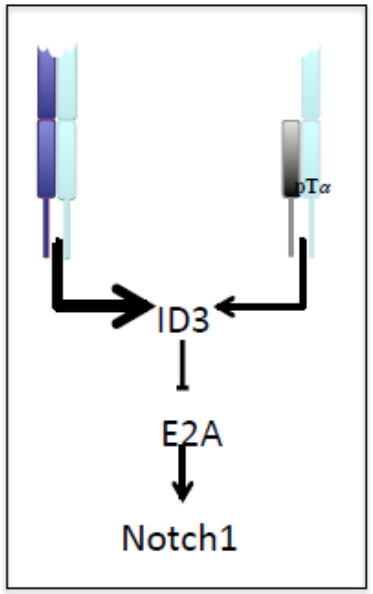
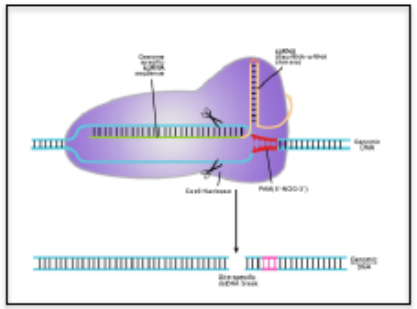
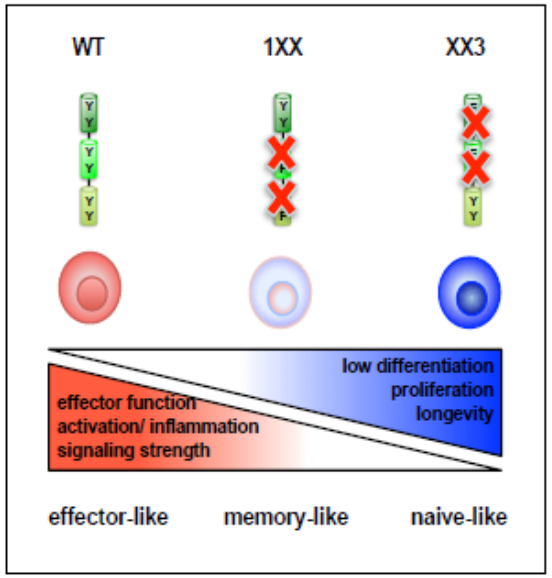
Removing the Barriers to DP Differentiation and SP Transition











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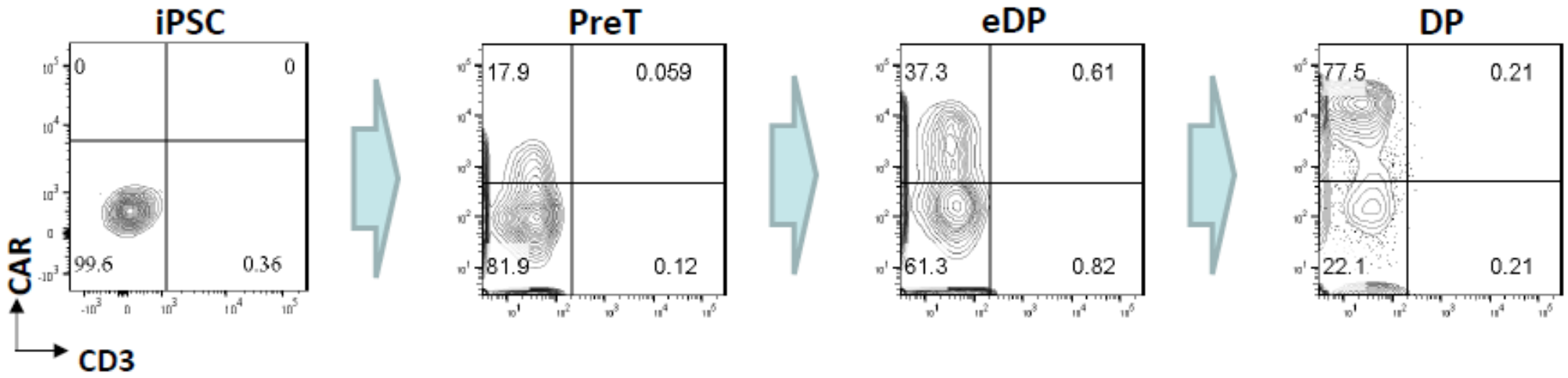
Temporal Regulation of CAR Expression in the Absence of TCR

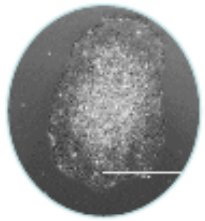


***TRAC* Regulated CAR Expression is Upregulated During Differentiation**

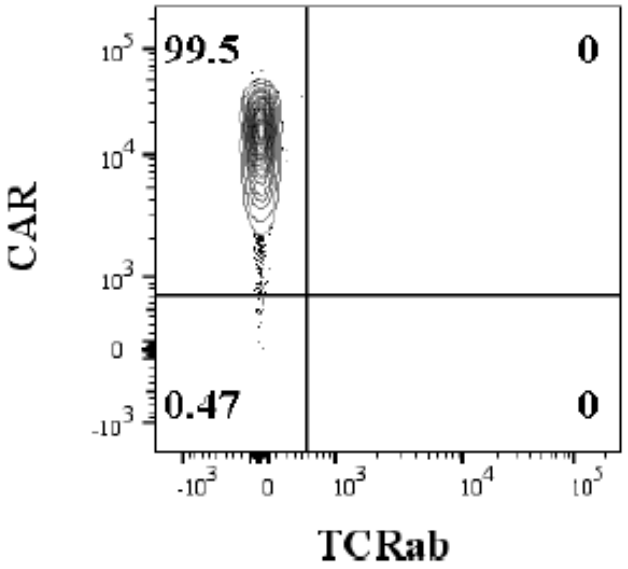
Memorial Sloan Kettering Cancer Center

FT819: iPSC-derived, TCR-less CAR19 T Cell Product Candidate

A First-of-Kind CAR T-cell Therapy



Renewable Engineered
Pluripotent Cell Line
[TCR-less, TRAC-CAR+]



FT819
TCR-less *TRAC*-CAR T cells

Master Cell Line Derived | Renewable
Homogenous | Efficacious
Cost-Effective | Multidose
Enabling

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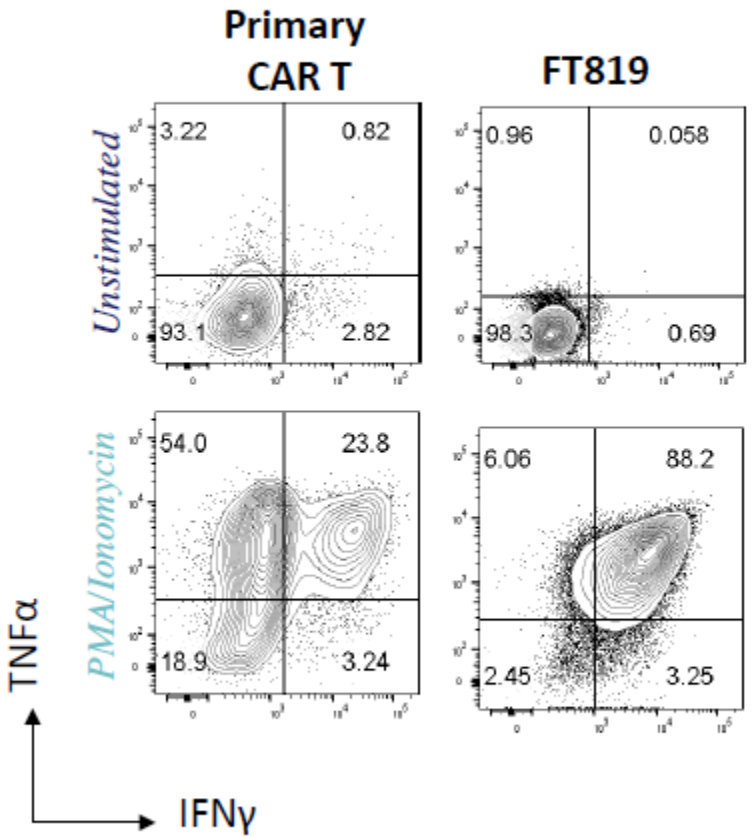
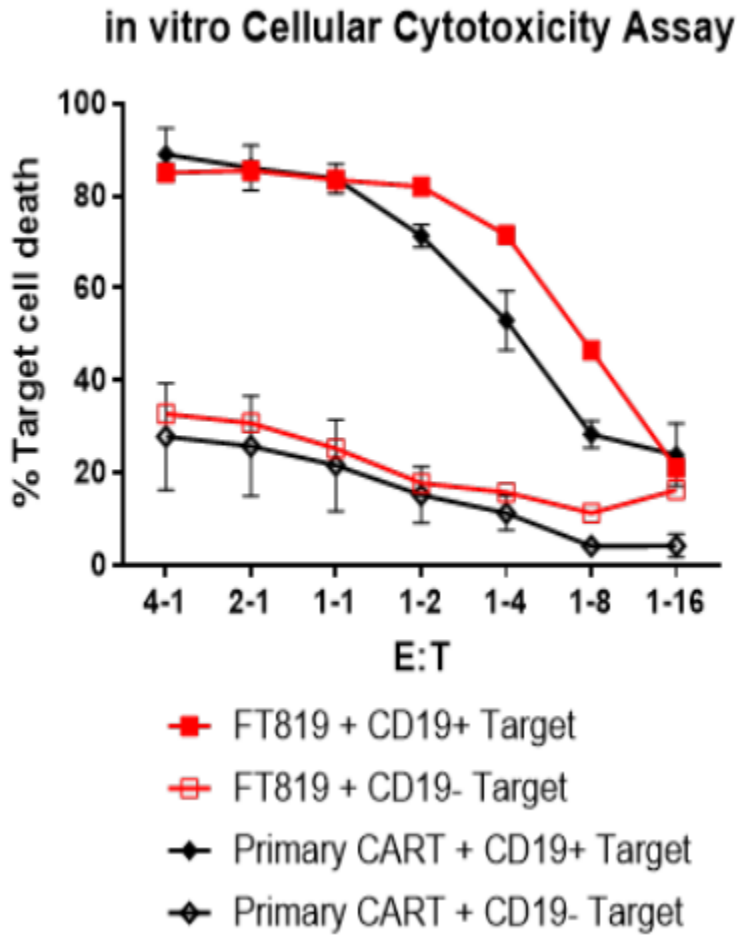
FT819: iPSC-derived, TCR-less CAR19 T Cell Product Candidate

In Vitro Cytokine Production and CD19 Antigen Specificity

Cytokine Production



Antigen-specific Cytotoxicity



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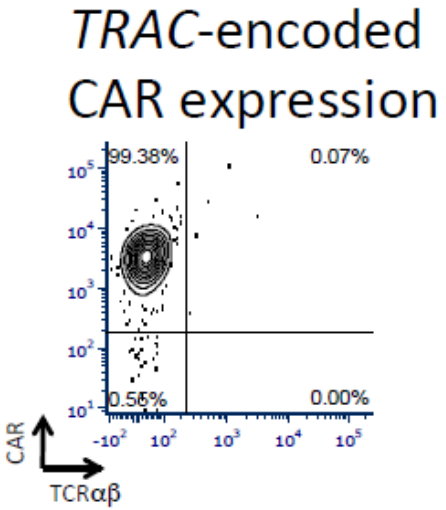
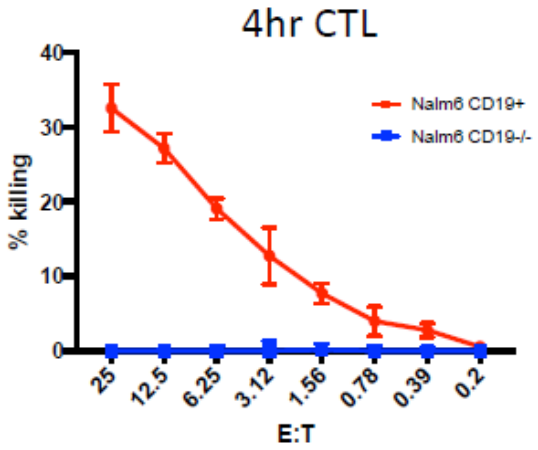
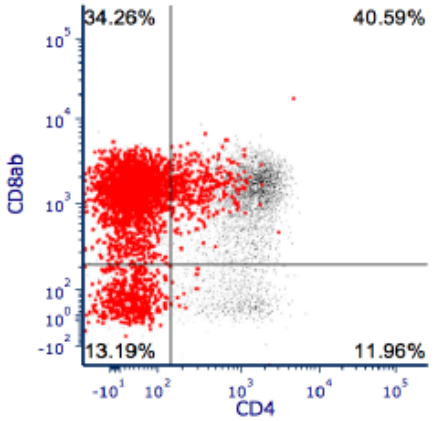
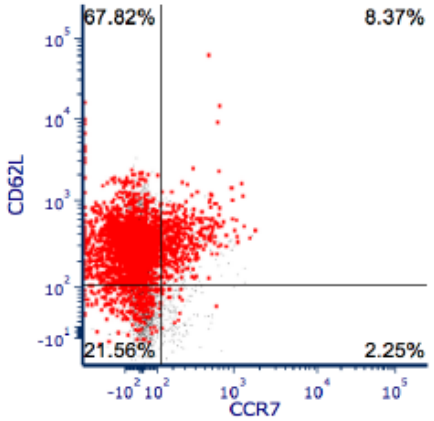
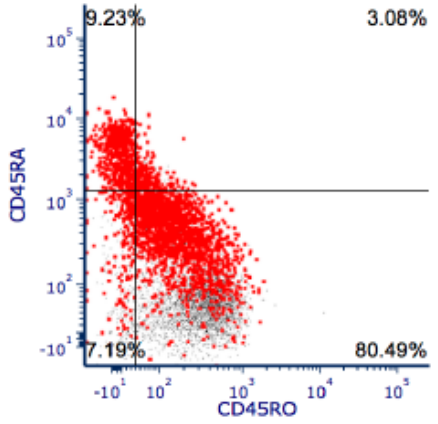
Display CD19-specific Toxicity and CD62L+ CCR7+ CD45RA+ Naive-like Phenotype











Stegen et al, unpublished

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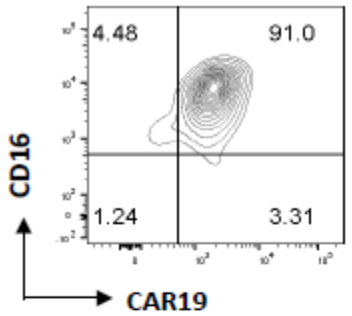
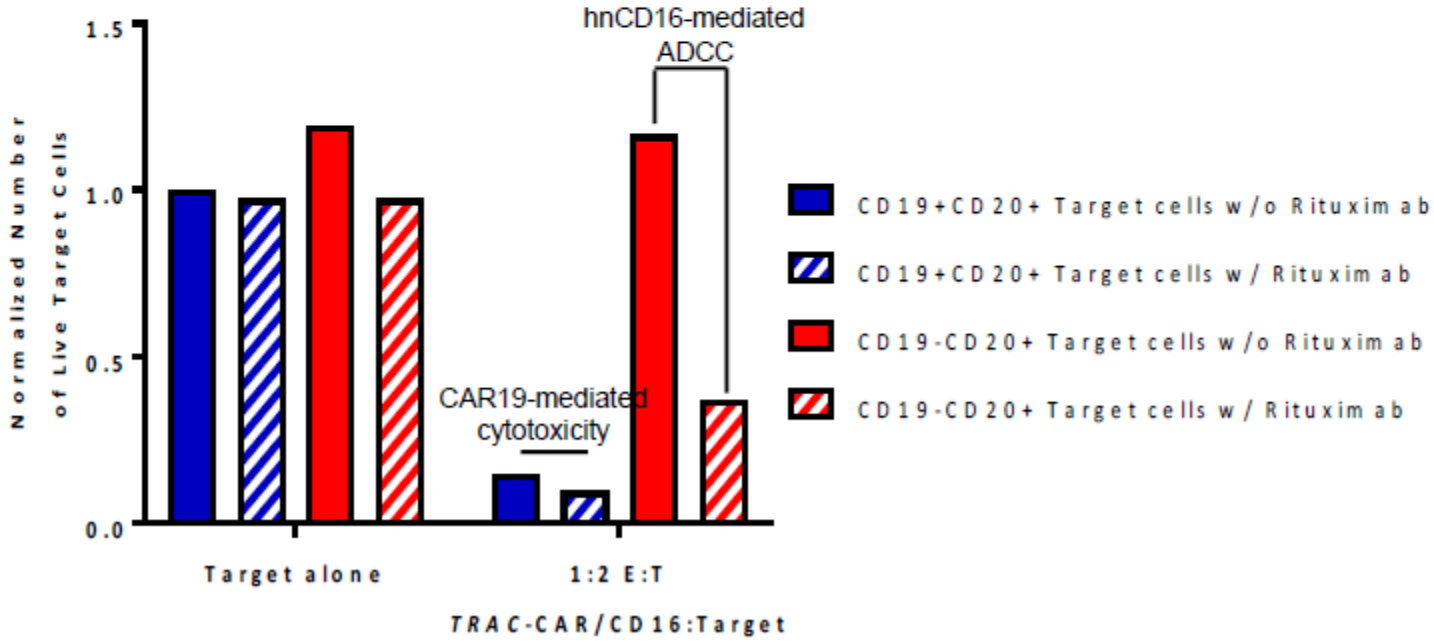
FT896: FT819 Engineered with hnCD16 Fc Receptor

Mitigating Antigen Escape through ADCC





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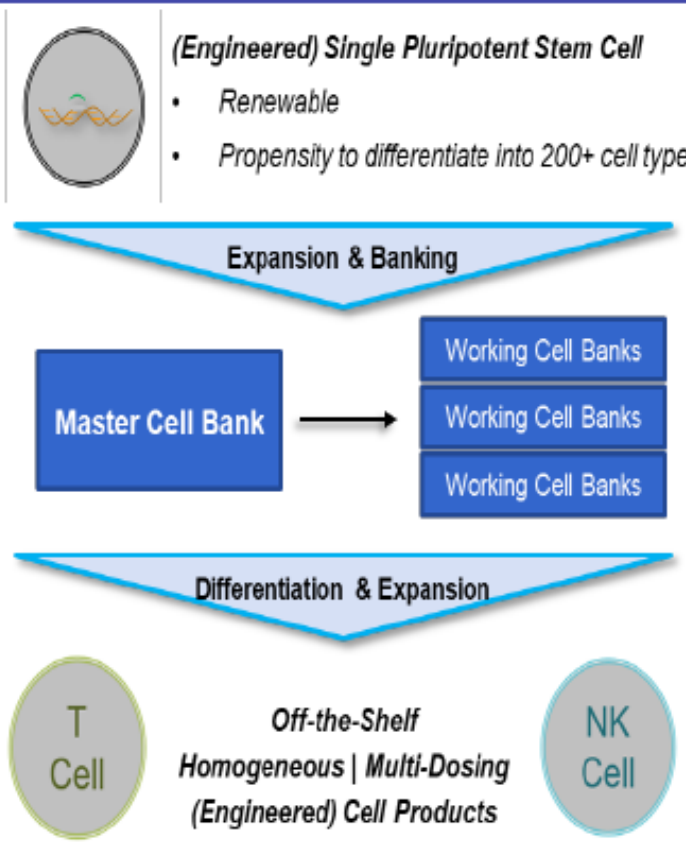
iPSC-derived, TCR-less CAR T Cells

A Paradigm Shift

Key Features	Cell Therapy 1.0	Cell Therapy 2.0
Cell Source	Patient Cells	*Single iPSC Clone*
Genetic Engineering	Random & Variable	
Product Consistency	Heterogeneous	
Characterization	Imprecise	*Unlimited Supply of Clonal iPSC Master Cell Lines*
Manufacturing	Personalized	
Delivery	Delayed & Uncertain	
Dose-per-Patient	Single	*Thousands of Clonally-derived Doses of Cell Products*
Overall Paradigm	**Patient-centric**	



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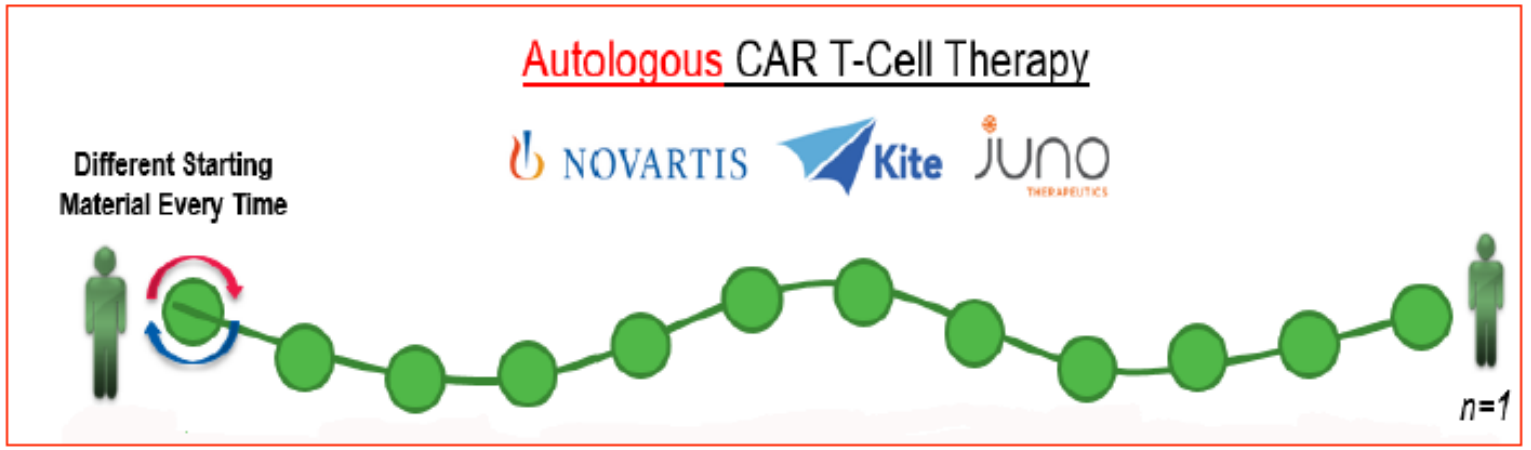
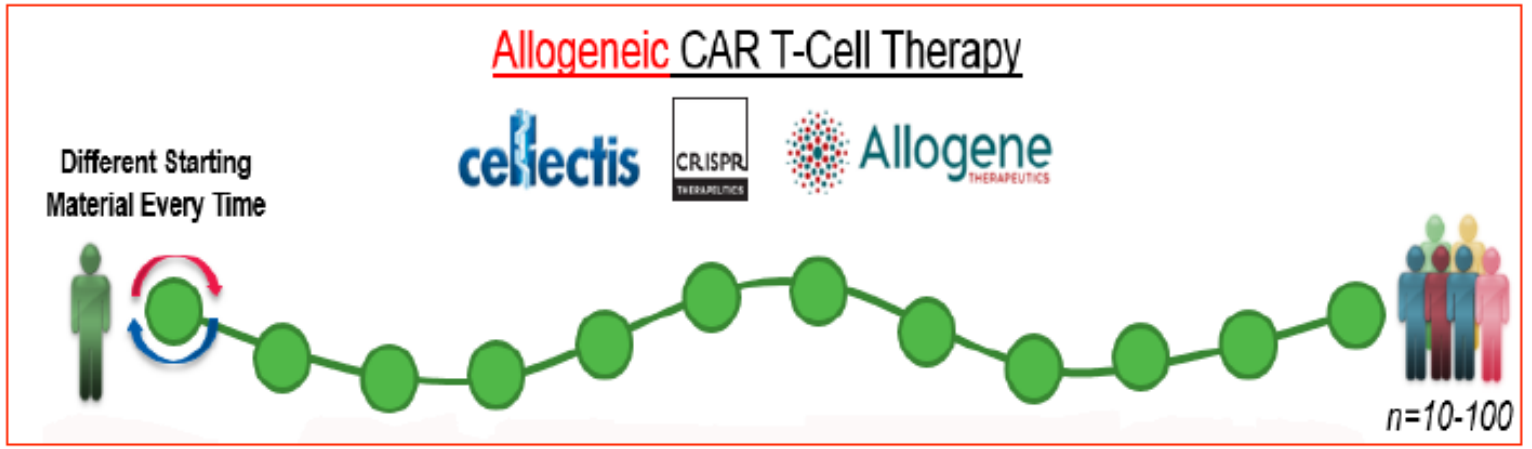
Patient- and Donor-derived CAR T-Cell Therapy





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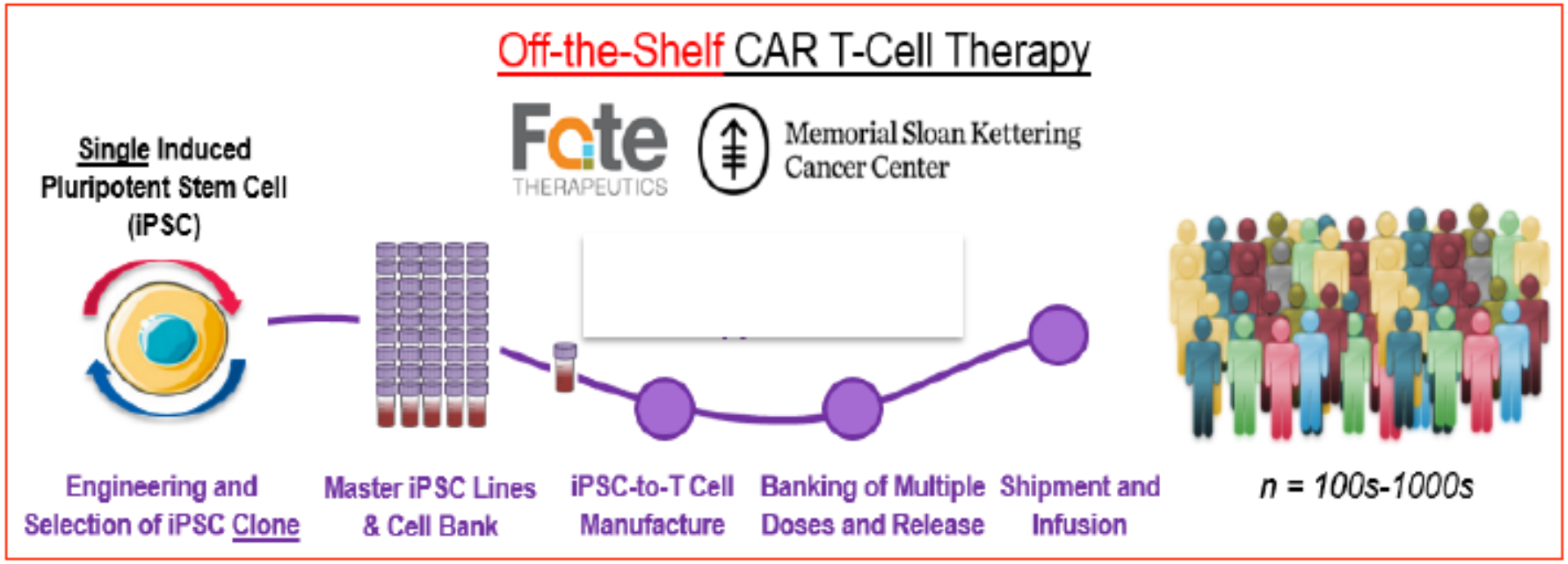
iPSC-derived, Off-the-Shelf CAR T-Cell Therapy



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Concluding Remarks

Scott Wolchko, President & CEO

iPSC-derived, Off-the-Shelf Cancer Immunotherapy Pipeline

	Description	R&D	Preclinical Dev	Process Dev	Manufacturing	IND Filing	Phase 1
Off-the-Shelf NK Cells (FT5xx)							
FT500	Allogeneic iNK + Check Point Inhibitors						
FT516	hnCD16 iNK (ADCC) + monoclonal antibodies						
FT596	CAR19 + hnCD16 + mbIL15 CD19 CARnk | USE | CIP						
FT538	CD38 KO + hnCD16 + mbIL15 + Daratumumab						
FT576	CAR-BCMA + hnCD16 + CD38 KO +/- Daratumumab						
FT5solid	CARsolid + USE + CIP + multifaceted engineered attributes						
Off-the-Shelf T Cells (FT8xx)							
FT819	TCRless TRAC-Targeted CAR19						
FT896	TCRless TRAC-Targeted CAR19 + USE						
FT817	TCRless TRAC-Targeted CAR-BCMA						
FT8solid	TCRless + TRAC-CARsolid + USE + multifaceted engineered attributes						

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University of Minnesota Driven to Discover℠

Oslo University Hospital

UC San Diego

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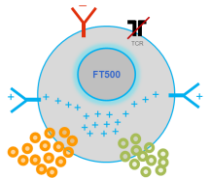
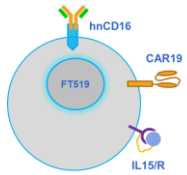
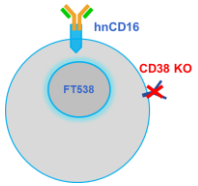
The Best Cancer Care. Anywhere.



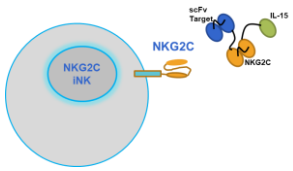
FT500 iPSC-Derived NK Cells and **Anti-PD1 Antibody Synergize** to Enhance T-Cell Cytokine and Cytolytic Responses Against Multiple Tumors



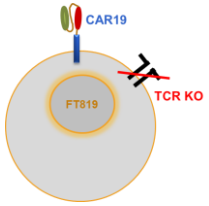
FT596 Off-the-Shelf Natural Killer Cells with Multi-Functional Engineering Using a Novel **Anti-CD19 Chimeric Antigen Receptor** Combined with Stabilized CD16 and IL15 Expression to Enhance Directed Anti-Tumor Activity



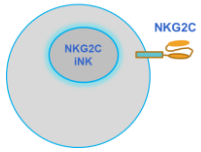
FT538 CD38 Deficient, CD16 Engineered NK Cells Exhibit Enhanced Antibody Dependent Cellular Cytotoxicity without NK Cell Fratricide to Augment Anti-Myeloma Immunity in Combination with Daratumumab



iPSC-Derived NK Cells **Genetically Modified to Express NKG2C/DAP12** Mediate Potent Function When Targeted through an NKG2C/IL15/CD33 **Tri-Specific Killer Engager**



FT819 Pluripotent Cell-Derived Off-the-Shelf TCR-Less **CAR-Targeted Cytotoxic T Cell** Therapeutic for the Allogeneic Treatment of B Cell Malignancies



FATE-NK100E: Efficient Scale-up and Pre-clinical Evaluation of **NKG2C+ Adaptive NK Cell** Expansion for **Therapy Against High-risk AML/MDS**

Better Cells For Better Therapies™