Kite Pharma

CIRM Webinar: CAR-T Cell Immunotherapy - Challenges and Opportunities Using Mature or Stem Memory T Cells, March 18th, 2015

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Forward Looking Statements / Safe Harbor

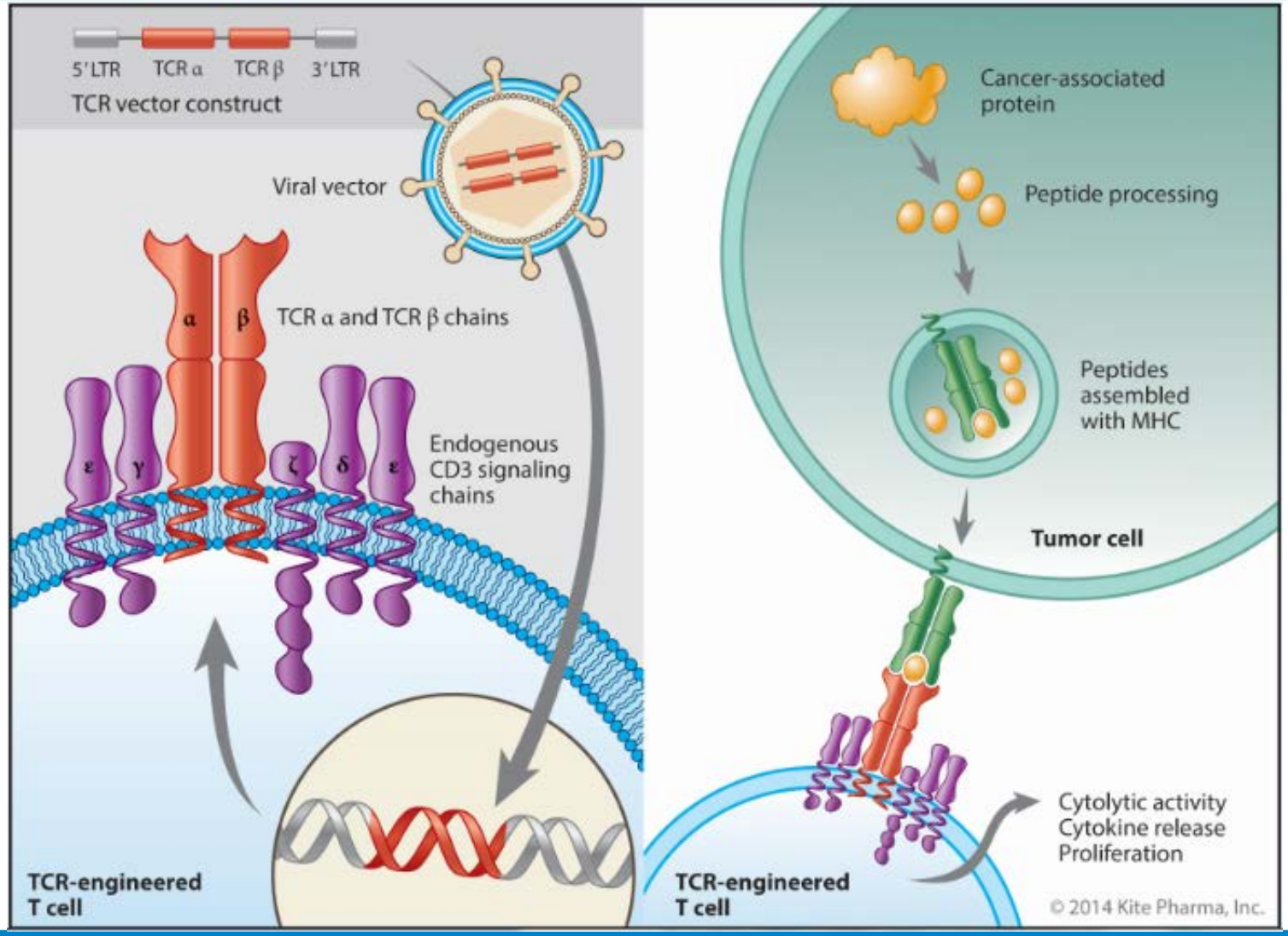
To the extent statements contained in this presentation are not descriptions of historical facts regarding Kite Pharma, Inc. ("Kite," "we," "us," or "our"), they are forward-looking statements reflecting management's current beliefs and expectations. Forward-looking statements are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry's actual results, levels or activity, performance, or achievements to be materially different from those anticipated by such statements. You can identify forward-looking statements by words such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes. Forward-looking statements contained in this presentation include, but are not limited to, statements regarding: (i) the success, cost and timing of our product development activities and clinical trials; (ii) the ability and willingness of the National Cancer Institute (NCI) to continue research and development activities relating to our product candidates; (iii) our ability to obtain and maintain regulatory approval of KTE-C19 and any other product candidates; (iv) the ability to license additional rights relating to product candidates and to comply with our existing license agreements; (v) our ability to obtain funding for our operations and further development and commercialization of our product candidates; (vi) the commercialization of our product candidates, if approved; (vii) our plans to research, develop and commercialize our product candidates; (viii) current and future agreements with third parties in connection with the research, development and commercialization and supply of product candidates; (ix) the size and growth potential of the markets for our product candidates, and our ability to serve those markets; (x) the rate and degree of market acceptance of our product candidates; (xi) our ability to attract and retain key scientific or management personnel; (xii) the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and (xiii) our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates. Various factors may cause differences between Kite's expectations and actual results as discussed in greater detail in Kite's filings with the Securities and Exchange Commission, including without limitation in its Form 10-Q for the quarter ended Sept. 30, 2014. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy securities, nor shall there be any sale of securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

Some of the views expressed herein are not made on behalf of Kite Pharma, Inc

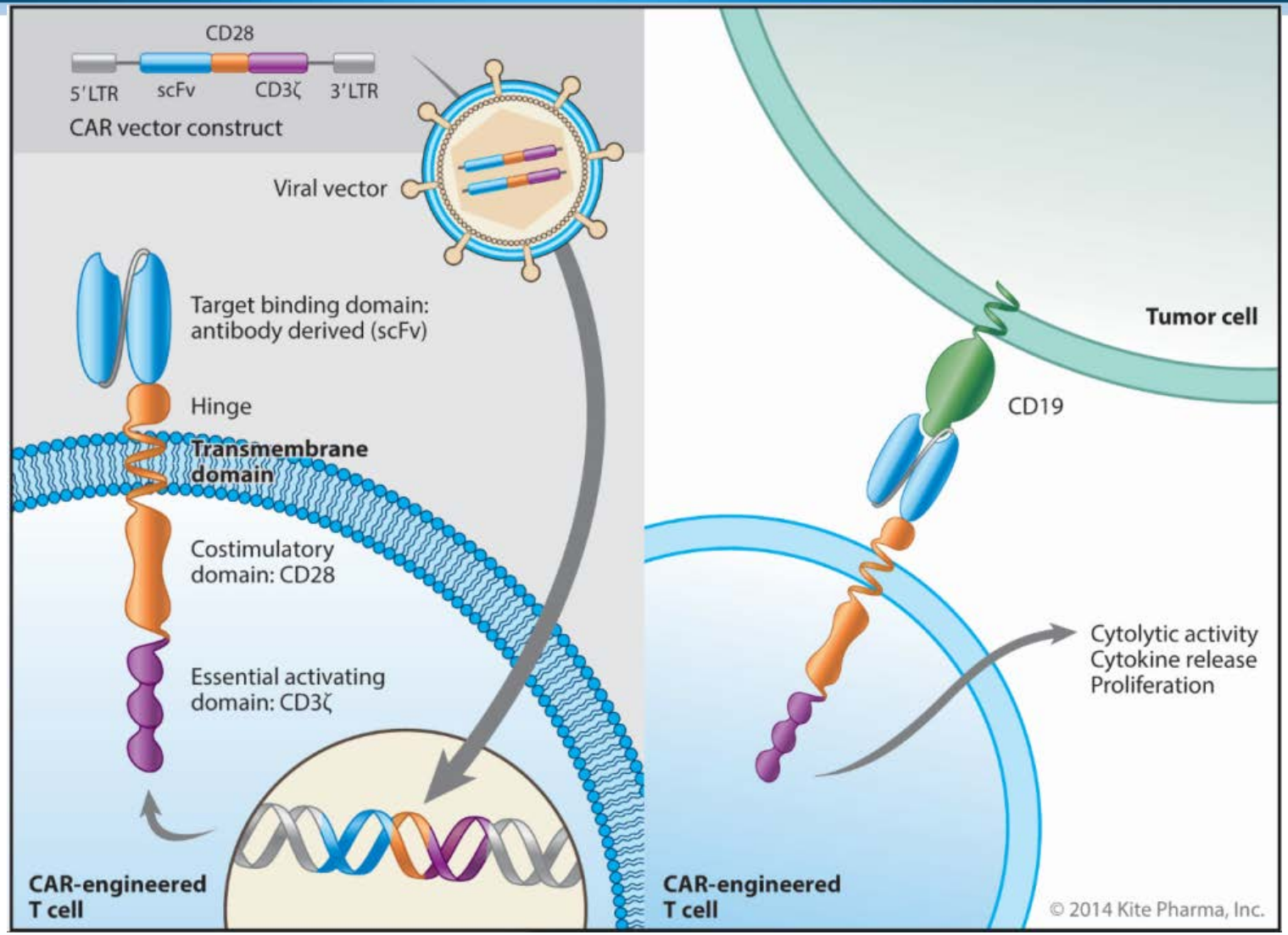
Primary Factors Influencing CAR T Cell Potency

- Manufacturing process
- Patient pre-conditioning regimen
- CAR Design

T Cell Receptor eACT

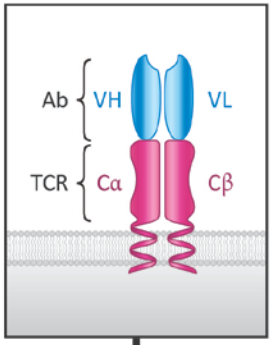


Chimeric Antigen Receptor eACT

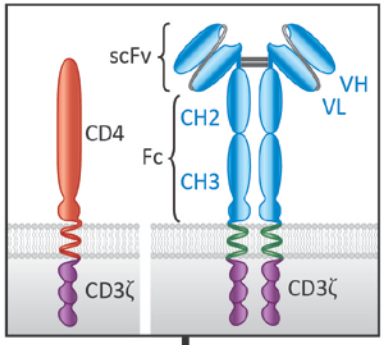


Evolution of the CAR Field: a 25 Year Odessey

Gross, 1989
Ab-TCR CAR



Roberts, 1994
1st gen anti-HIV CARs: preclinical study
CD4ζ scFv-based CAR

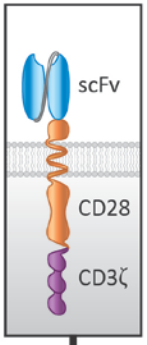


Kershaw, **2000**
Clinical trial with 1st gen anti-folate receptor CAR

Lamers, **2006, 2007**
Clinical trial with 1st gen CAR anti-CA-IX CAR

Walker, **1996**
Clinical trial with 1st gen anti-HIV CAR: CD4ζ

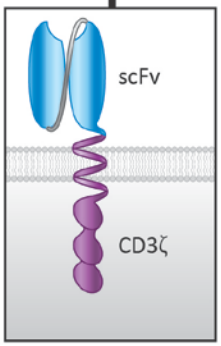
Kochenderfer, 2010
Clinical trial with 2nd gen CAR (α-CD19)



1989 1991 1993 1994 1995 1996 2010

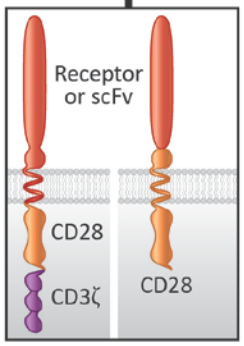
Irving & Weiss, **1991**
CD8ζ CAR: proof of concept

Romeo & Seed, **1991**
CD4ζ CAR: anti-HIV



Eshhar, 1993
scFv-CAR

Stancovski; Hwu; Gross, 1993
Anti-tumor CAR

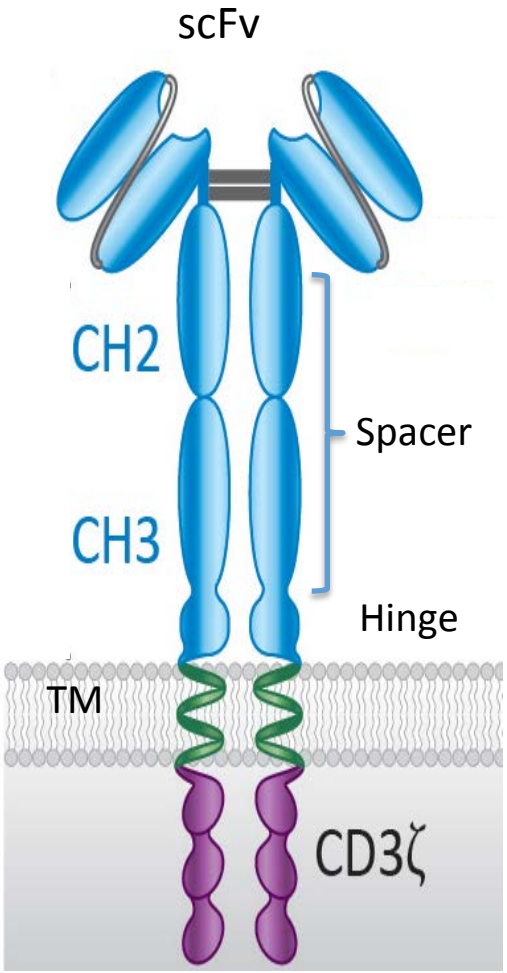


Roberts, 1995
US 5712149 2nd gen CAR

Alvarez-Vallina & Hawkins, **1996**
scfv-CD28

Krause, **1998**: scFv-CD28;
Finney, **1998**: 2nd gen scFv-CAR

CAR Design - 1st Generation Essential features



I: TM & extracellular domain

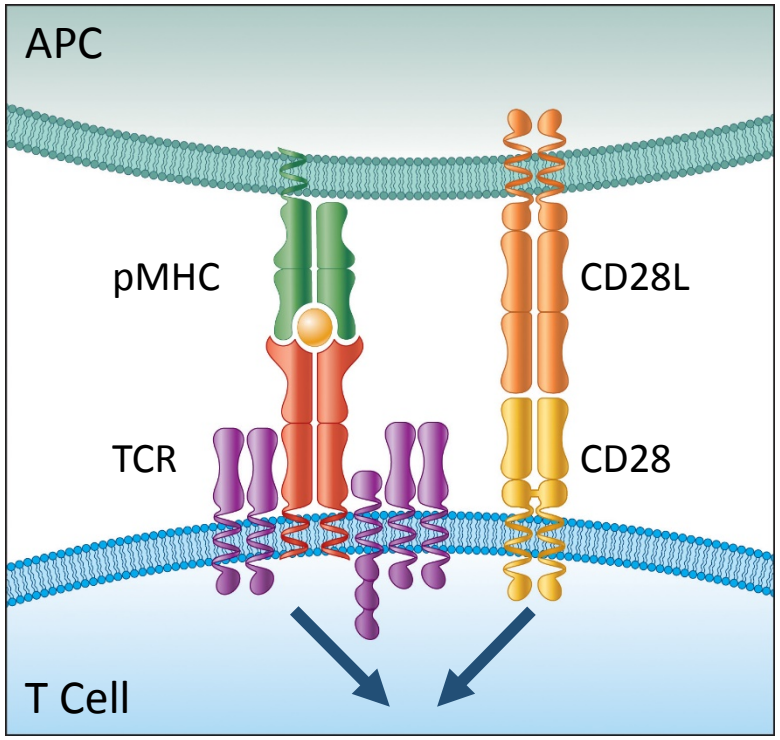
- Spacer/Fc domain
  - Distance between T cell and target cell plasma membranes at immunological synapse (TCR-pMHC complex formation) ~ 135 A
  - Requirement for/length of spacer (e.g. IgG Fc domain) is CAR scFv-epitope specific
- Hinge
  - Provides appropriate flexibility for CAR-target epitope binding
  - Derived from members of Immunoglobulin Superfamily (IgSF)
  - Potential for covalent homodimer formation via conserved Cys
- Transmembrane domain (TM)
  - Derived from IgSF TM proteins that participate in immunological synapse; independent of other proteins for surface expression

II: Signaling domain

- Cytoplasmic domain of TCR CD3ζ chain provides essential signal 1 via ITAM adaptors

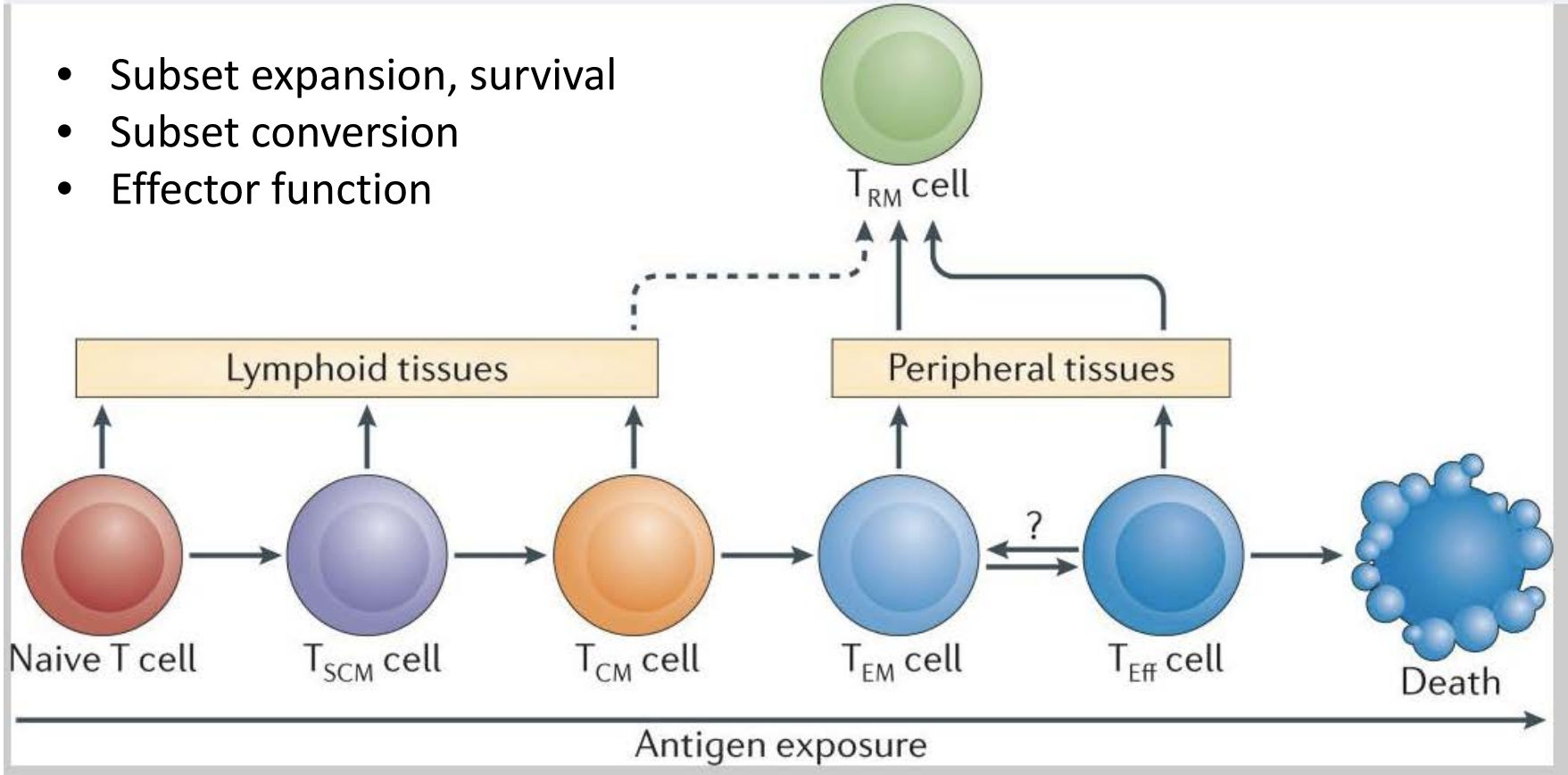
Role of Co-stimulatory Receptors
Concept of Signal 2

- Signal 1: TCR-pMHC
  - TCR/CD3ζ ITAMS
- Signal 2: Co-signaling receptors
  - Stimulatory
  - Inhibitory
- Costimulatory receptors regulate
  - **Memory-effector T cell subsets**
  - Proliferation and survival
  - Polarization of effector T cells
- Two major superfamilies
  - Ig superfamily
    - CD28, CD2/SLAM, B7, TIM, CD226
  - TNFR superfamily



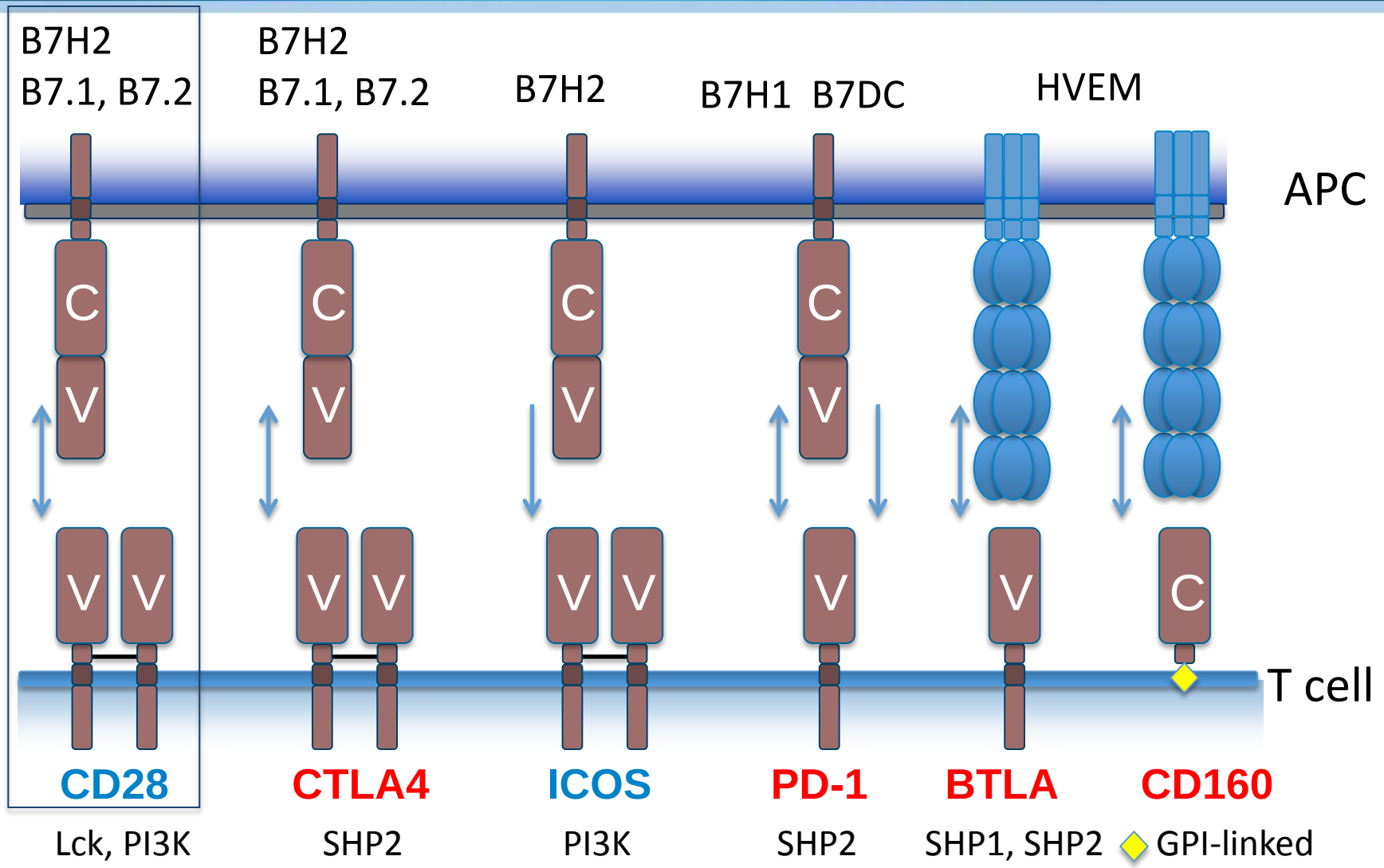
Role of Costimulatory Receptors in Regulation of Human T Memory, Expansion & Survival

- Subset expansion, survival
- Subset conversion
- Effector function

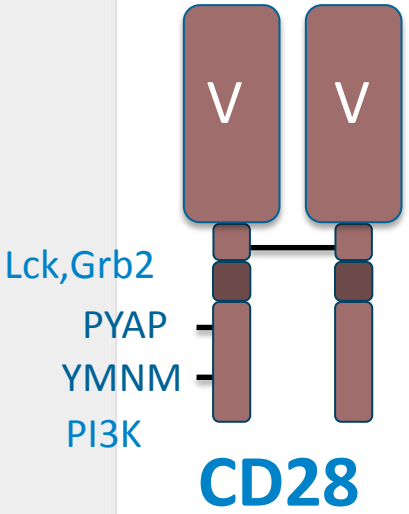


Farber et al., Nat Rev Immunol 2014 14:24

CD28 Family of Co-signaling Receptors

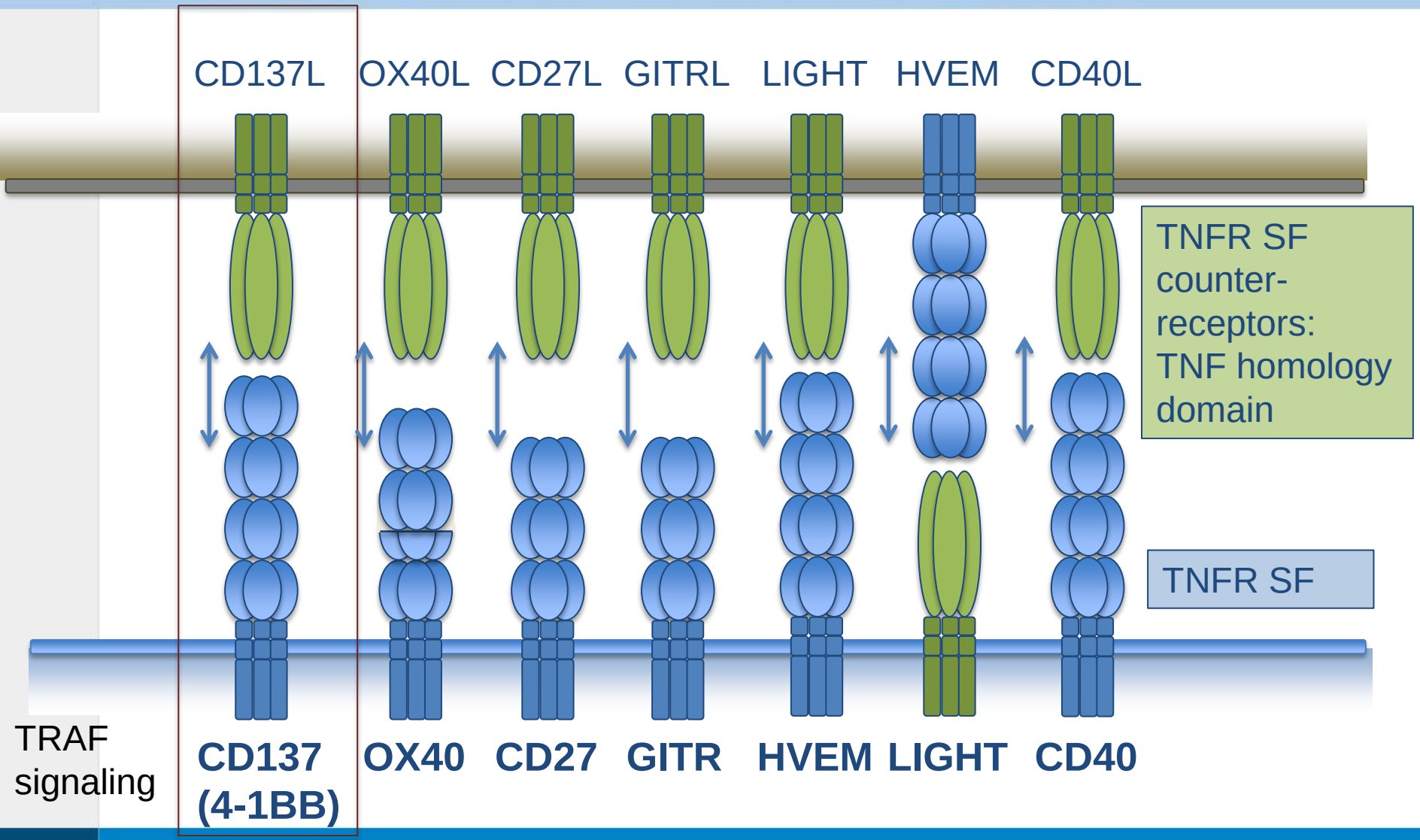


CD28 Costimulatory Function

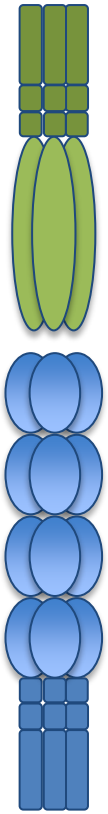


- Constitutively expressed on naïve & memory subsets
  - Naïve, Tscm, Tcm, Tem
  - Ligands induced on APC –EARLY
- Naïve T cells
  - Essential for naïve T cell activation
- Major prosurvival and proliferative role
  - Induces IL-2 production and T cell proliferation
  - Protects against antigen-induced cell death and anergy
- Memory subsets
  - Major role in Tcm expansion; CM→EM conversion
- Acts as a TCR signal amplifier
  - Mitogenic activity requires TCR, CD3ζ, Zap70
    - No TCR-pMHC independent activity in response to natural ligand

TNFR Superfamily of Co-signaling Receptors



41BB Costimulatory Function



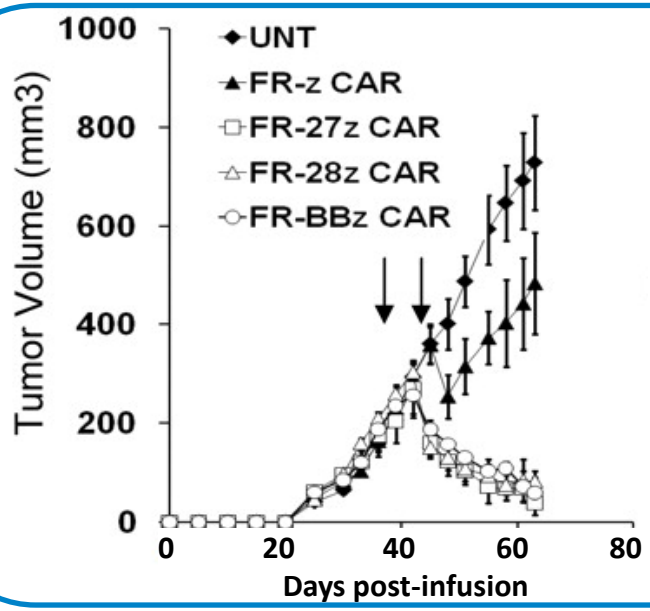
CD137 (4-1BB)

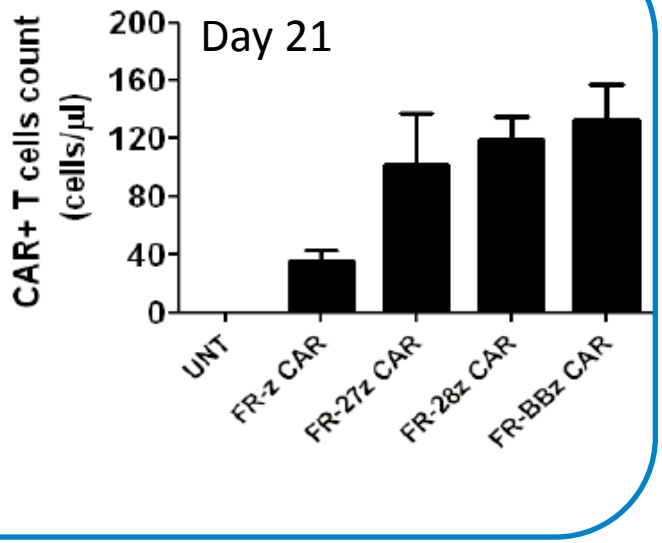
- Expression induced during late phase of T cell activation
  - Transiently induced on activated T cells (GITR-dependent?)
  - CD137L induced on APC
  - Induced on Tcm cells by IL-15 and IL-2 in vitro
- No role in naïve T cell priming
- Drives CD8 Tcm expansion/maintenance
  - TCR activation-/antigen-independent expansion – unlike CD28
  - Does not induce IL-2
  - Proximal signaling pathways distinct from TCR/CD3, CD28 & ICOS
  - Distal pathways partially overlapping
  - More dramatic impact on CD8s compared to CD4s

CAR Design: Second Generation
Inclusion of Co-stimulatory Domain

- Drives temporal association of CD3ζ signal 1 and costimulatory signal 2
- Compensates for lack of costimulatory ligand expression on non-hematologic solid tumors, and down-regulation of costimulatory receptors on T cells
- Enhances T cell persistence, expansion and anti-tumor activity in setting of hematologic malignancies, despite expression of costimulatory ligands
  - Kowolik et al., 2006 *Cancer Res* 66: 10995 [CD28-CAR vs 1st gen in mouse]
  - Savoldo et al., 2011 *J Clin Invest* 121: 1822 [CD28-CAR vs 1st gen in human]

2nd Gen CAR: Impact of Costimulatory Domain on Potency and Persistence





Song D et al. Blood 2012;119:696-706

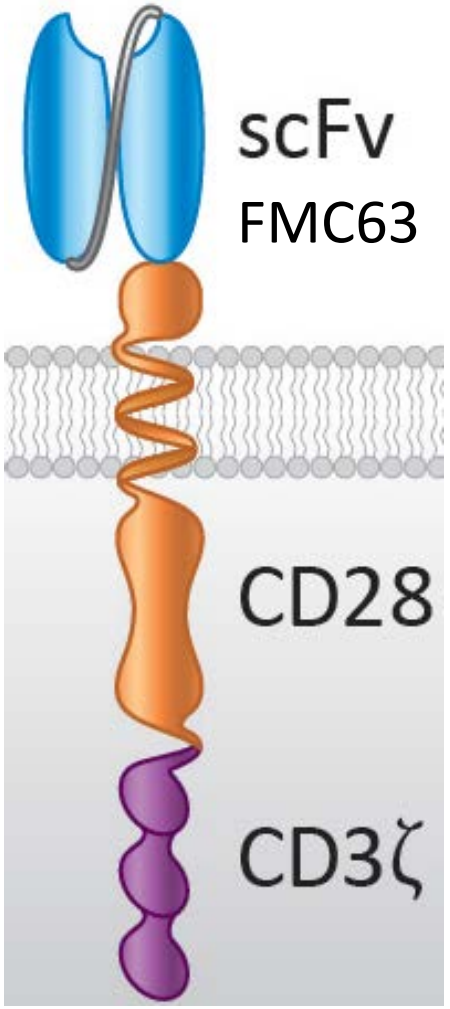
Folate receptor (FR)-specific CARs:

- FR-ζ
- FR-CD27ζ
- FR-41BBζ
- FR-CD28ζ

- As expected, anti-tumor activity 2nd gen CARs dramatically superior to 1st gen ζ only
- No significant difference in anti-tumor activity of different 2nd gen CAR T cells
- No significant difference in blood frequency of 2nd gen CAR T cells @ 3 weeks
- Impact of costimulatory (and other) domains on CAR T cell effector functions, memory subset formation/survival in blood & tumor under investigation

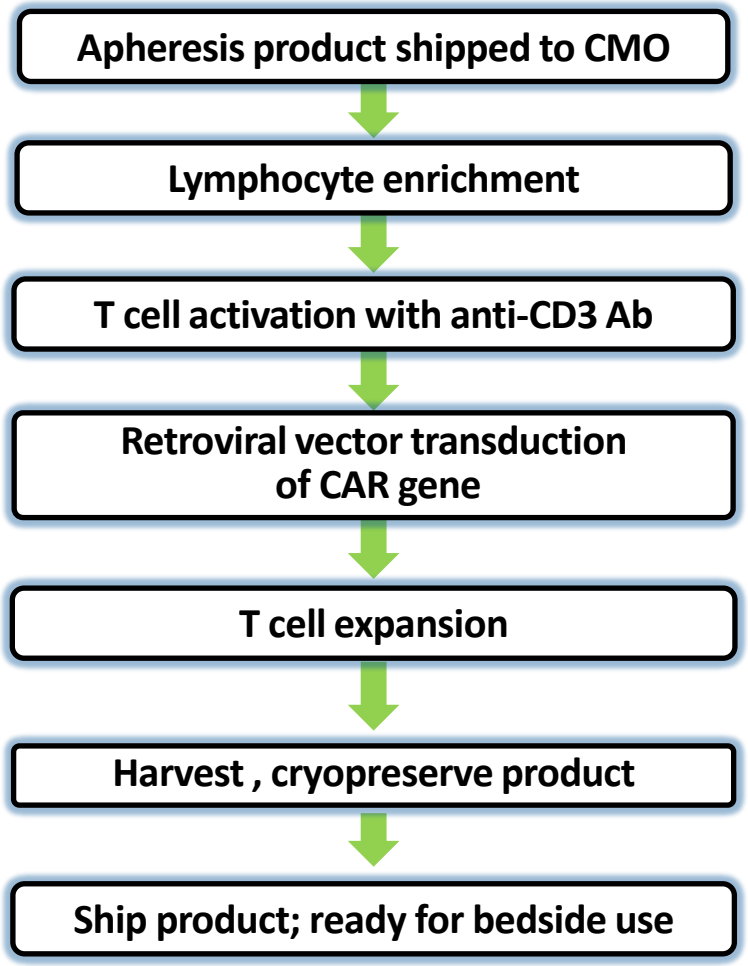
Kite/NCI Study of anti-CD19 CAR in Relapsed/Refractory B-Cell Malignancies

- Phase 1/2 study investigating safety, feasibility, and efficacy
  - DLBCL, PMBCL, CLL, Indolent NHL
- Refractory/recurrent disease incurable by standard therapy
- Evolving treatment protocol (conditioning/dosing)
- 10-day manufacturing process → reduced to ~ 1 week



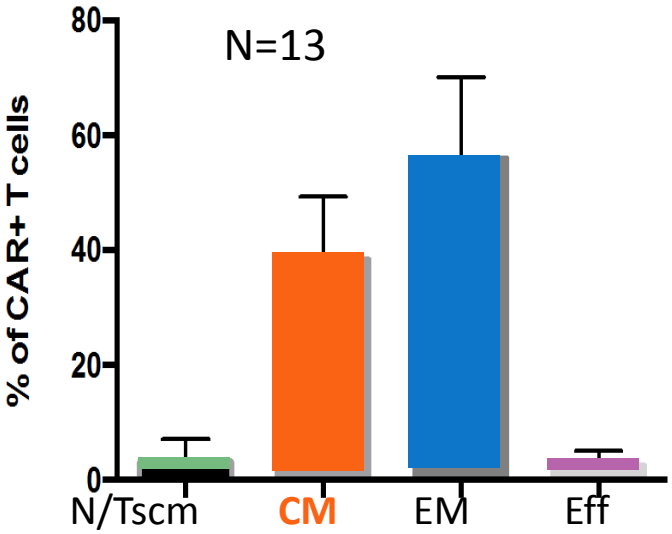
Kochenderfer Blood 2012; Kochenderfer JCO 2014; Kochenderfer ASH 2014

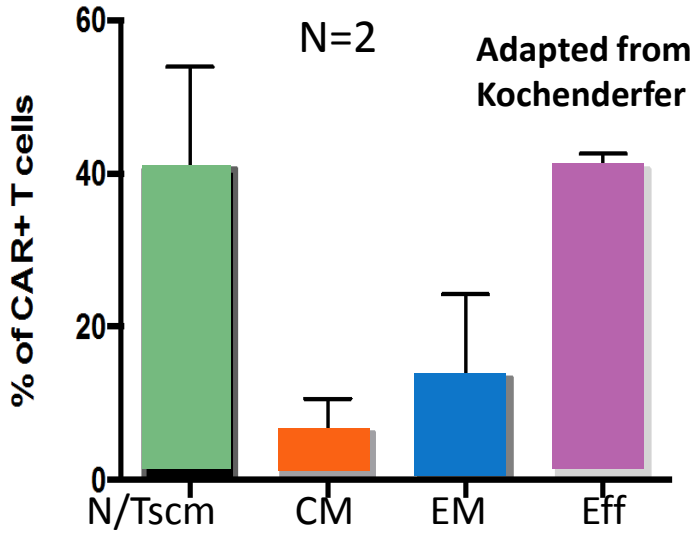
Streamlined and Rapid eACT ™ Manufacturing Process for anti-CD19 CAR T Cells (KTE-C19)



- Single T cell stimulation of PBMC in human serum-free media
- Streamlined process amenable to cGMP
- Progenitor Cell Therapy (PCT) to manufacture clinical supply
- Kite developing additional clinical and commercial manufacturing facilities
- Transportation logistics in place for KTE-C19 multi-center clinical trial

Kite/NCI Phase1/2
Memory Subset Composition of 10-Day Product





Adapted from:
Kochenderfer et al., 2014 JCO

- CAR+ Tcm present at ~40% in 10-day product for 13/15 patients
- Peak frequency CAR+ T cells in blood observed at day 7-17 post transfer
- Impressive clinical response
  - 8 CR, 4 PR, 1 stable, out of 13 evaluable patients
- Potential for reconstitution normal B cells
  - Retreat if necessary
- Extensive immunophenotypic analysis of patient product and blood samples underway

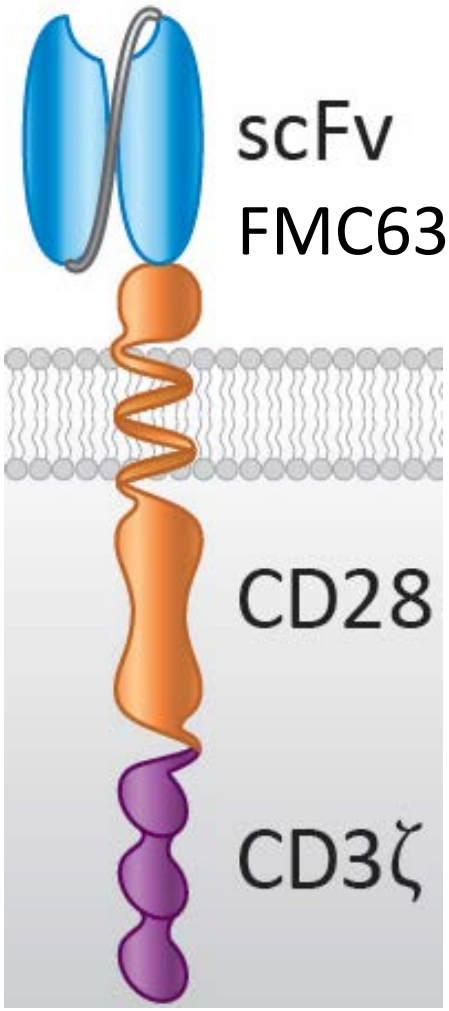
Kochenderfer JCO 2014

Kite/NCI Study of anti-CD19 CAR in Relapsed/Refractory B-Cell Malignancies: Phase 1/2

- 32 adult patients enrolled (29 evaluable); largest dataset of anti-CD19 CAR in lymphoma

Tumor Type (n evaluable)	Overall Response Rate	Complete Response Rate
Any (29)	76%	38%
DLBCL/PMBCL (17)	65%	35%
CLL (7)	86%	57%
Indolent NHL (5)	100%	25%

- 16 patients still in response; 12 ongoing > 1 year
- 3 patients were re-treated after progression; all in ongoing response (17+ to 52+ months)



Updated 12/2014

Kochenderfer Blood 2012; Kochenderfer JCO 2014; Kochenderfer ASH 2014

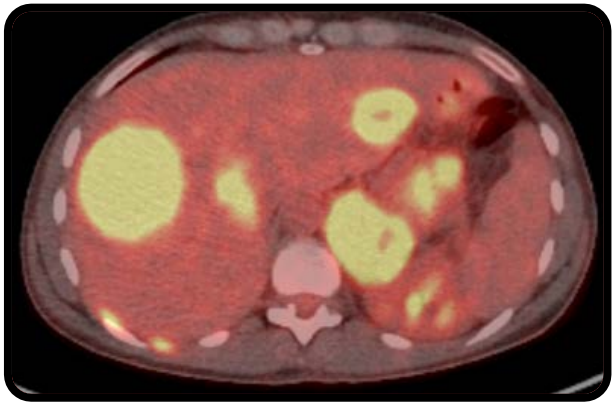
Complete Response in Patient with Chemotherapy Refractory PMBCL

Primary Mediastinal Large B-Cell Lymphoma

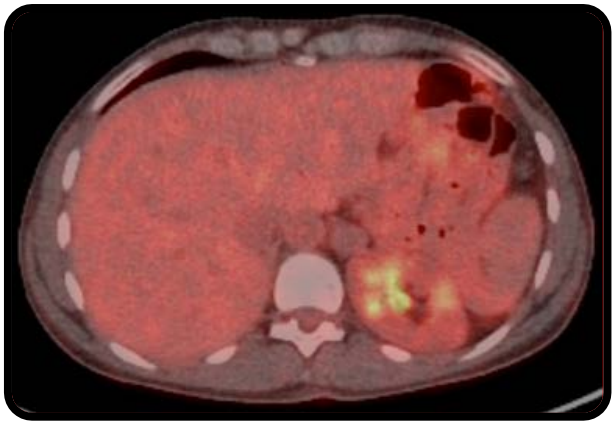
- Primary refractory
- Progressed on R-CHOP, R-ICE, and R-GDP
- Referred for progressive liver and other abdominal lymphoma

Ongoing Complete Response 15+ months

Prior to treatment



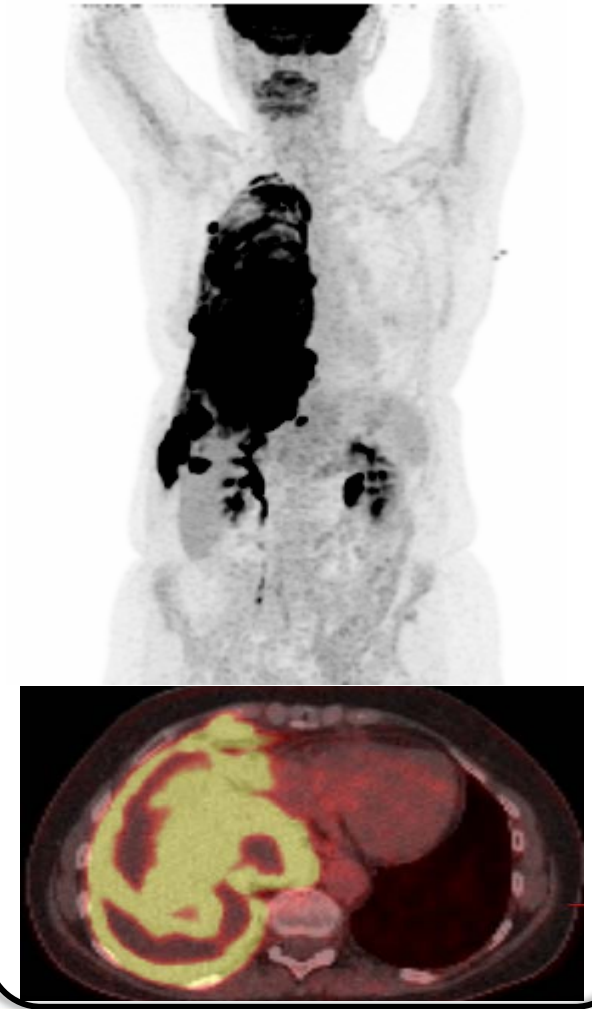
9 months post-treatment



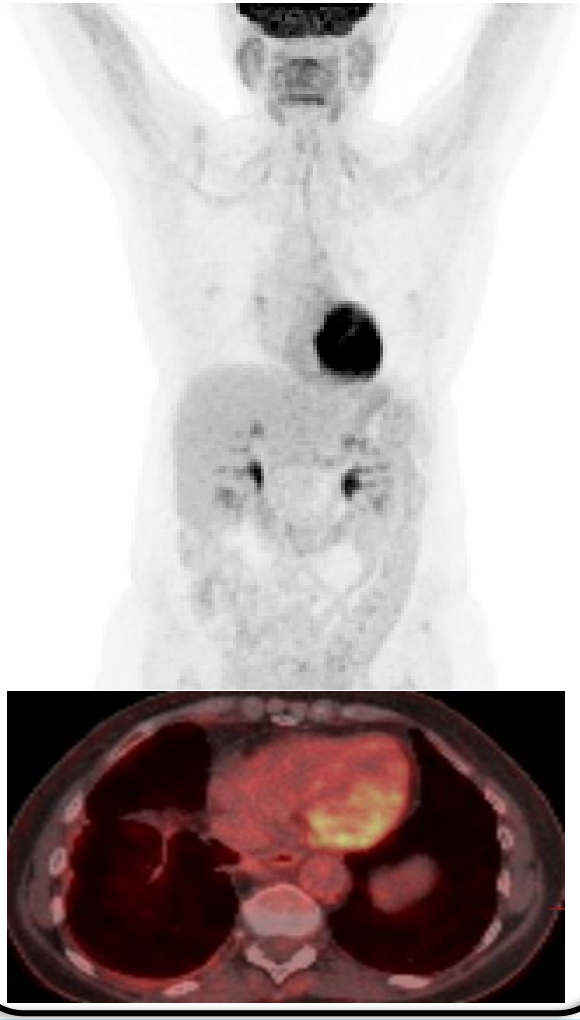
Scans from Dr. Rosenberg NCI

Patient with Refractory DLBCL

Prior to treatment



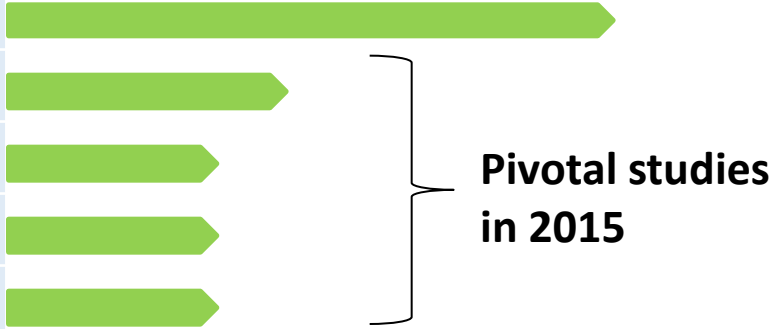
6 months post-treatment



Scans from Dr. Rosenberg NCI

Kite's CAR & TCR Product Pipeline

PROGRAM	INDICATION	PRE-IND	PHASE 1	PHASE 2/3
Anti - CD19 CAR	B Cell Malignancies			
KTE-C19 CAR	NHL (DLBCL)			
	NHL (MCL)			
	CLL			
	ALL			
EGFRvIII CAR	Glioblastoma			
NY-ESO-1	Various tumors			
HPV 16 E6	Cervical / Head & Neck Cancer			
HPV 16 E7				
MAGE A3/A6	Various tumors			
MAGE A3	Various tumors			
Neo-antigen	Various tumors			
SSX2	Various tumors			
Amgen Multi-Target CAR Collaboration	Heme Malignancies/ Solid Tumors			



Blood Cancers

Solid Tumors

*Targets and target # undisclosed

Kite CAR T Cell Product Development

- Key attributes of optimal CAR T cell product
  - Robust CAR expression
  - Minimal tonic signaling
  - Efficient multifunctional T cell activation in response to antigen
  - Durability of response and/or ability to retreat
  - Relatively straightforward manufacturing process
- Manufacturing process
  - KTE-C19: streamlined, rapid process
  - In addition, developing new processes for eACT products
- CAR Design
  - High throughput characterization and selection of optimal TM/hinge/spacer domains
  - Rational selection of costimulatory domain
- *Next generation eACT*

Next Generation eACT