ENGINEERED T CELL THERAPIES:

DEVELOPMENT, ACCESS, FUTURE PROSPECTS

Bruce L. Levine, Ph.D.

Dept. Pathology and Laboratory Medicine, Center for Cellular Immunotherapies, University of Pennsylvania

Co-Founder, Tmunity Therapeutics & Co-Founder, Capstan Therapeutics

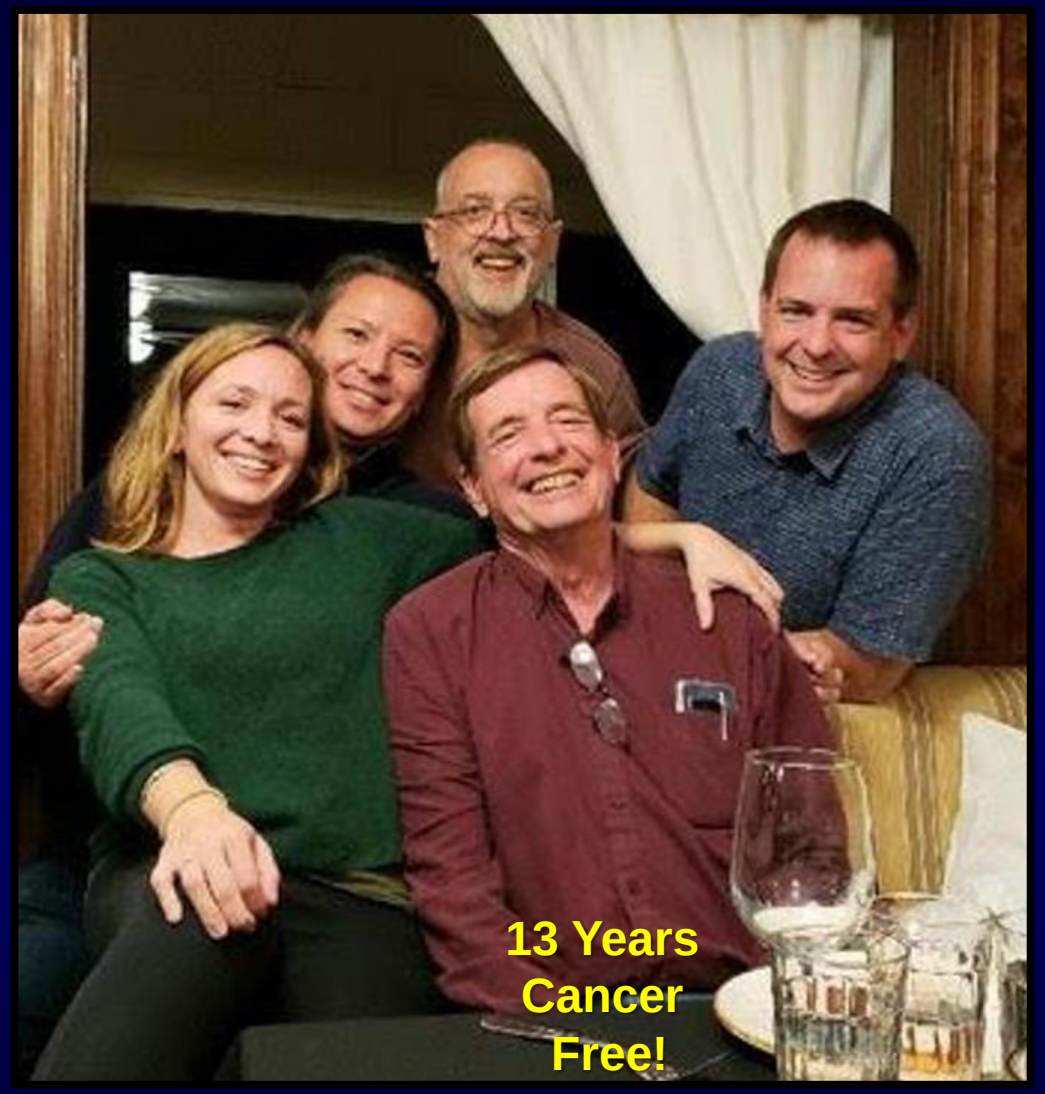
Past-President, International Society for Cell and Gene Therapy

@BLLPHD

Conflict of Interest Statement

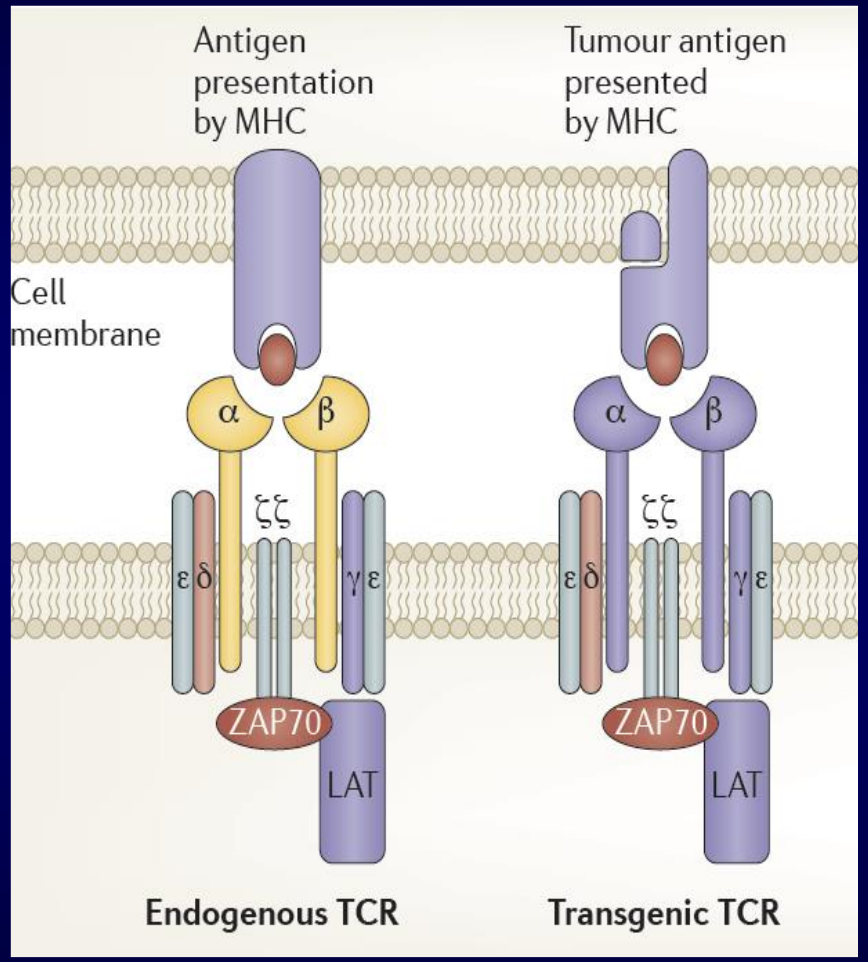
- Declaration of financial interest due to intellectual property and patents in the field of cell and gene therapy.
- Co-Founder and equity holder: Tmunity Therapeutics (acquired by Kite), Kite Senior Advisor, Capstan Therapeutics – Chair, SAB
- Scientific Advisory Boards: Akron, Avectas, Cellula Therapeutics, Immuneel, Immusoft, In8bio, Ori Biotech, Oxford Biomedica, ThermoFisher Pharma Services, UTC Therapeutics, Vycellix
- Conflict of interest is managed in accordance with University of Pennsylvania policy and oversight

How did we get here?



Where are we going?

Overcoming the Scarcity of Tumor Specific Immunity and Tumor Suppression: Creation of Re-directed T cells



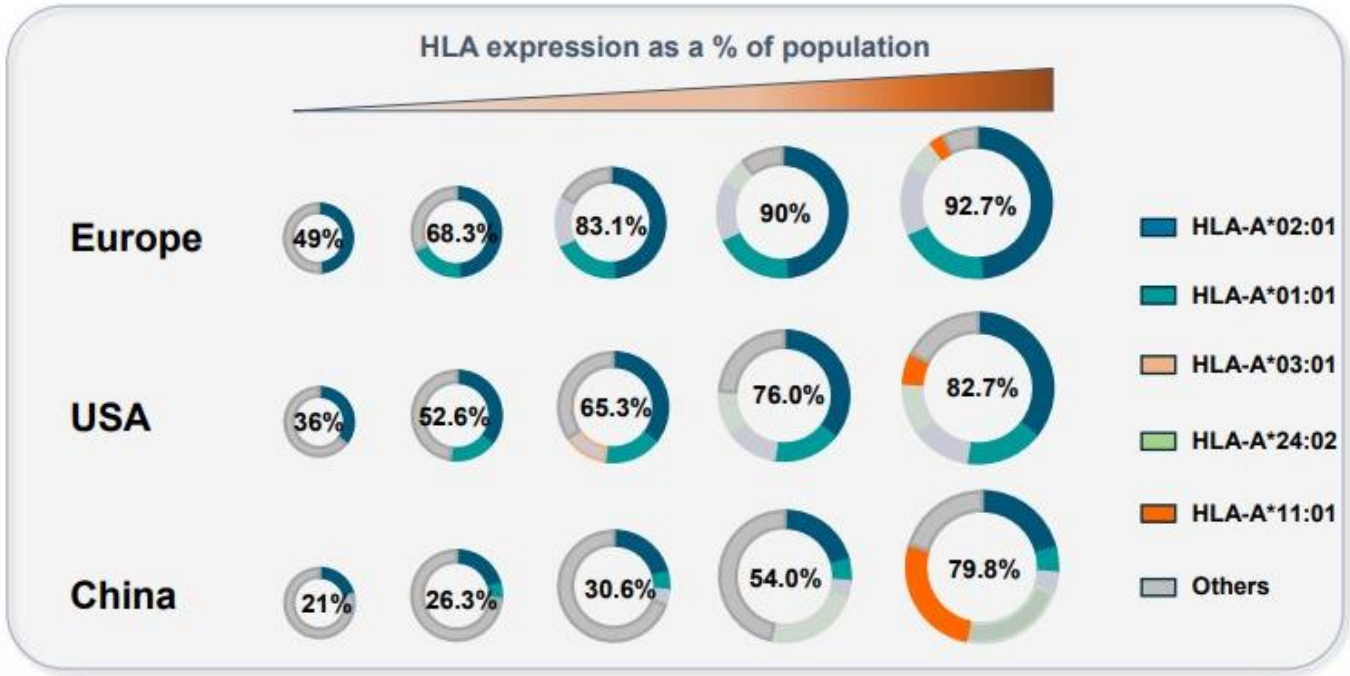
-intracellular Ags
-MHC dependent

Fesnak, June, Levine; Nature Reviews Cancer; Aug, 2016

Engineered T Cell Receptor Population Challenges

Key Target Challenges – Tumor Heterogeneity and Population Diversity

TCR library helps to address tumor heterogeneity in the broadest possible population



Multiple *HLAs* for single antigen / epitope

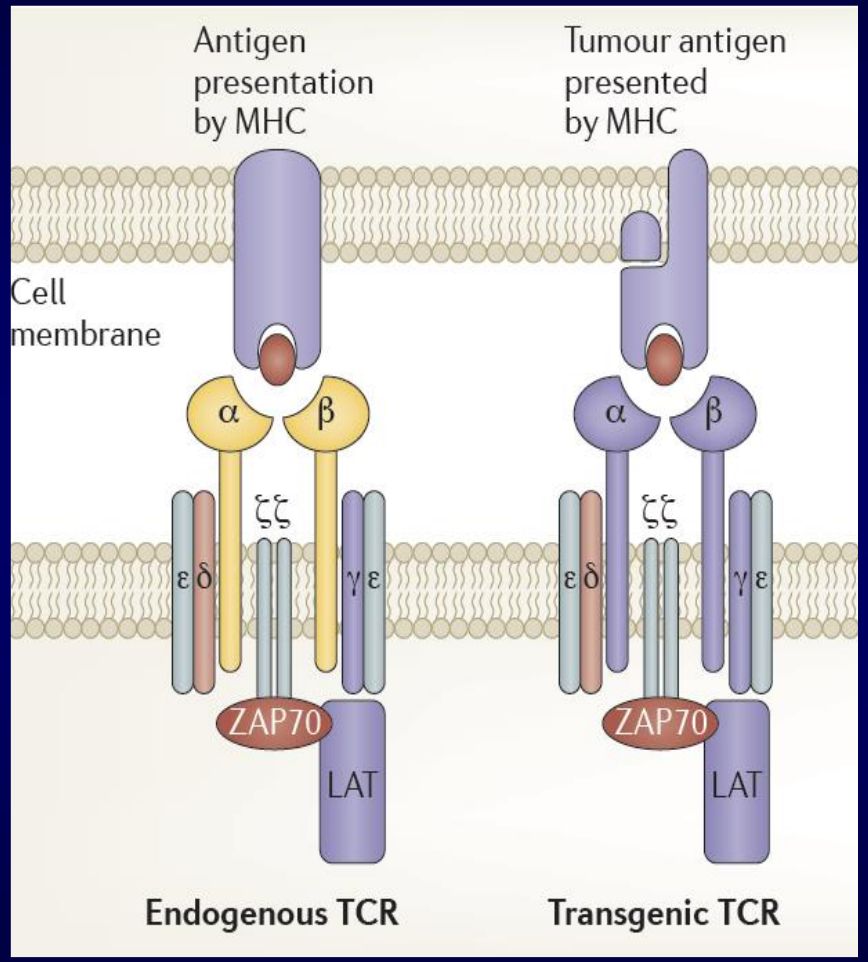
e.g. A*11 & A*03 for KRAS mutations
A*02 subtypes for NY-ESO-1 + LAGE-1a

Multiple *epitopes* for single HLA

e.g. A*11 for KRAS G12V, G12D….

medigene

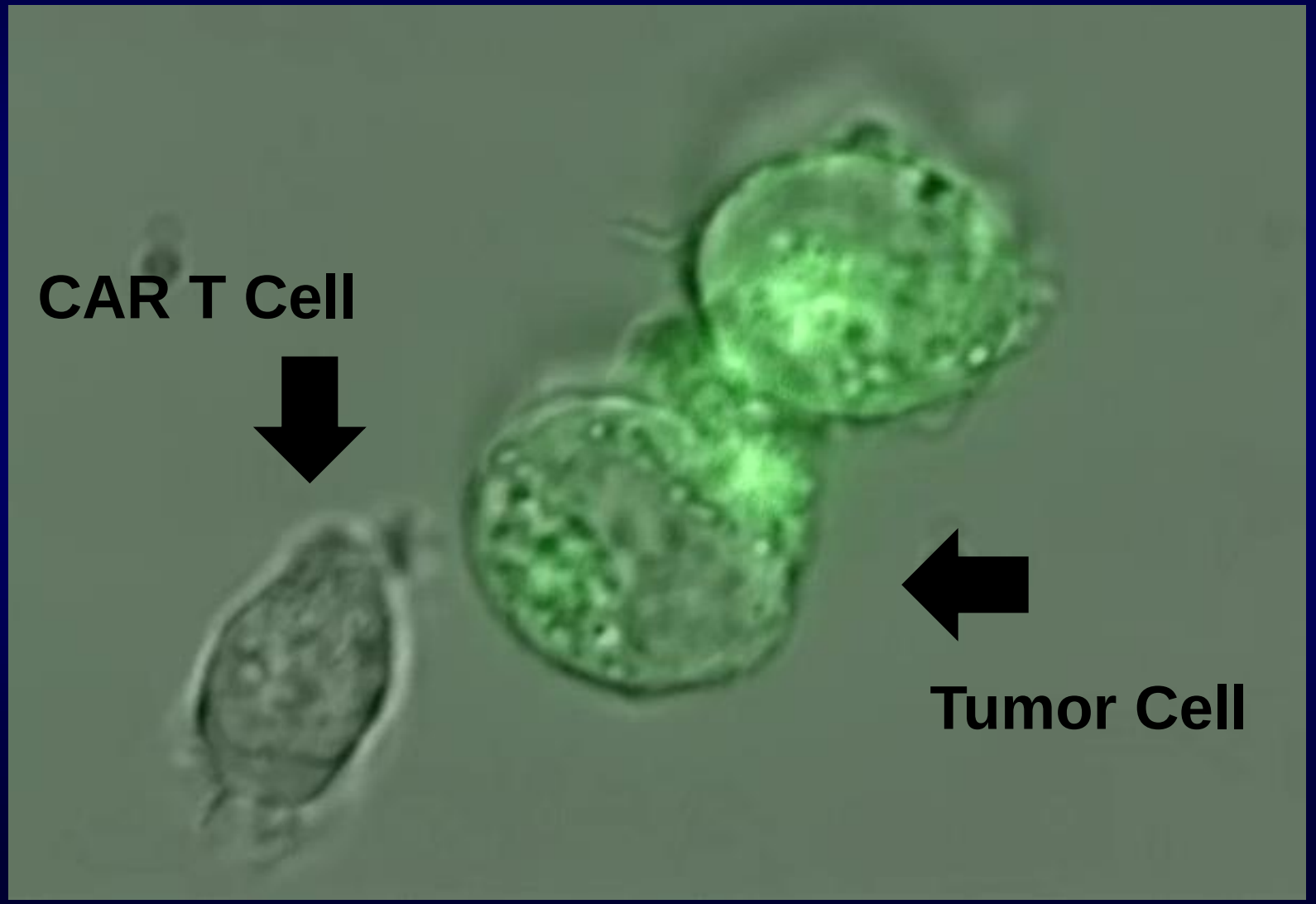
Overcoming the Scarcity of Tumor Specific Immunity and Tumor Suppression: Creation of Re-directed T cells



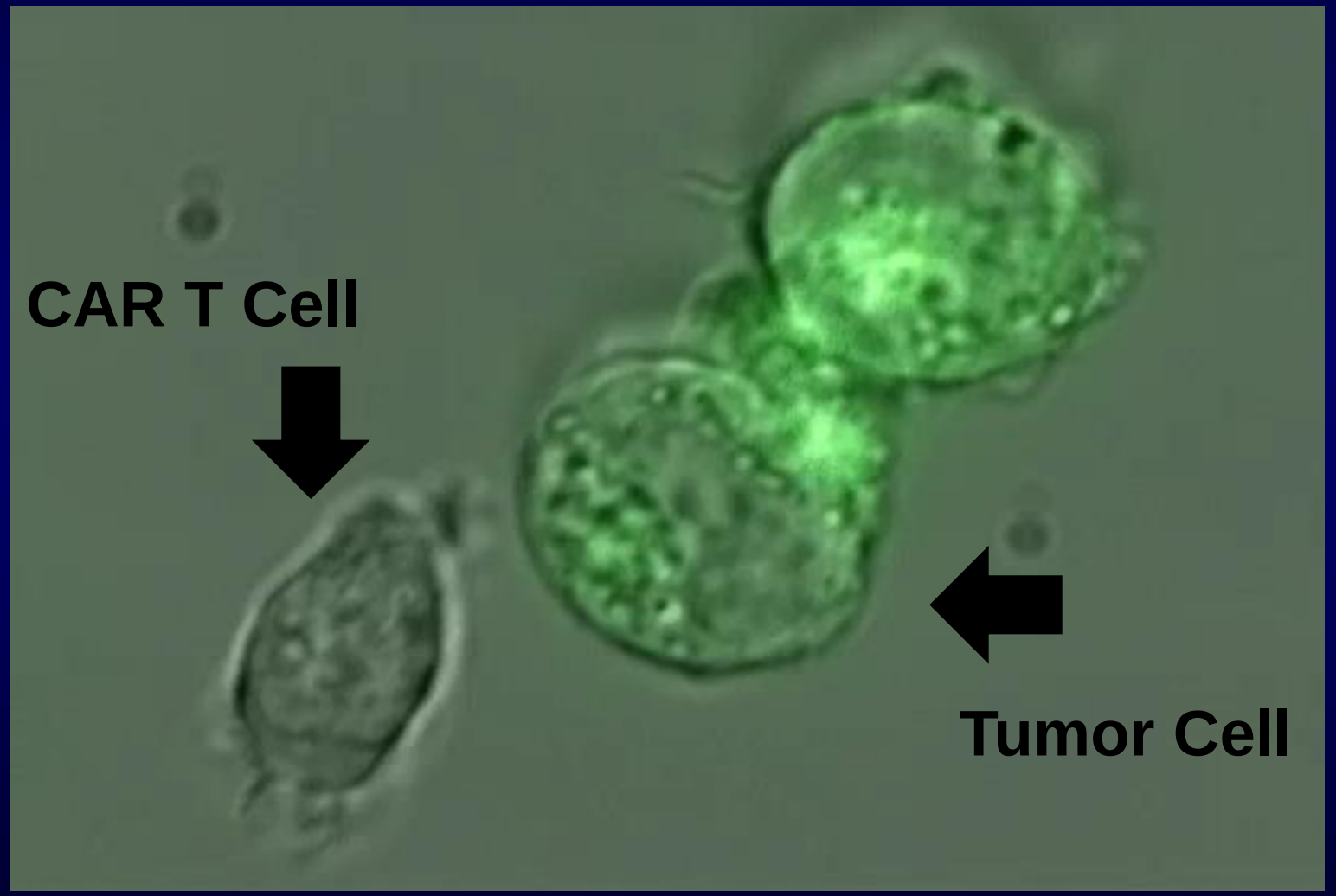
-intracellular Ags
-MHC dependent

Fesnak, June, Levine; Nature Reviews Cancer; Aug, 2016

Engineered Immunity:
Chimeric Antigen Receptor (CAR) T Cells To Kill Cancer

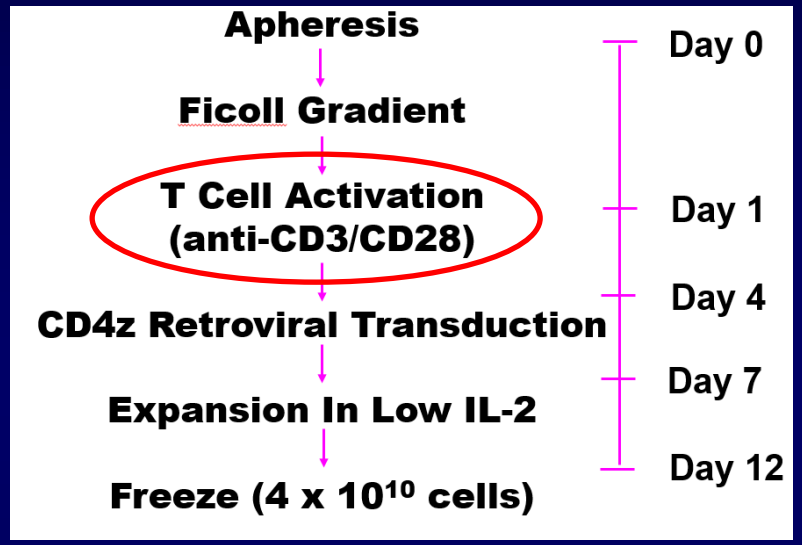


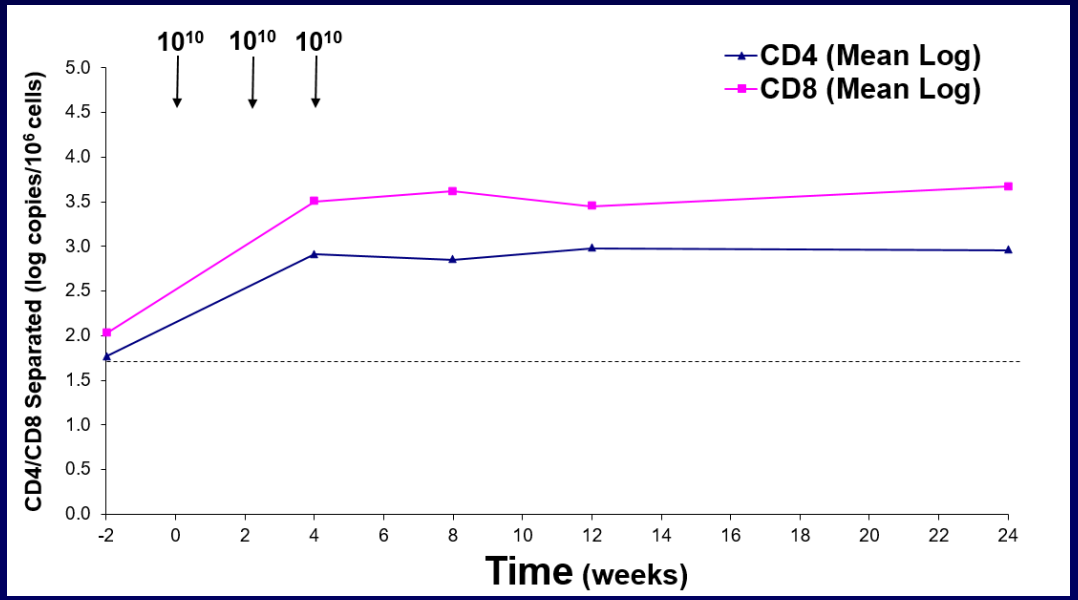
Engineered Immunity:
Chimeric Antigen Receptor (CAR) T Cells To Kill Cancer



Improved Persistence of CD4z-modified CD8 CAR T Cells

Now Manufactured With Anti-CD3/Anti-CD28 Beads



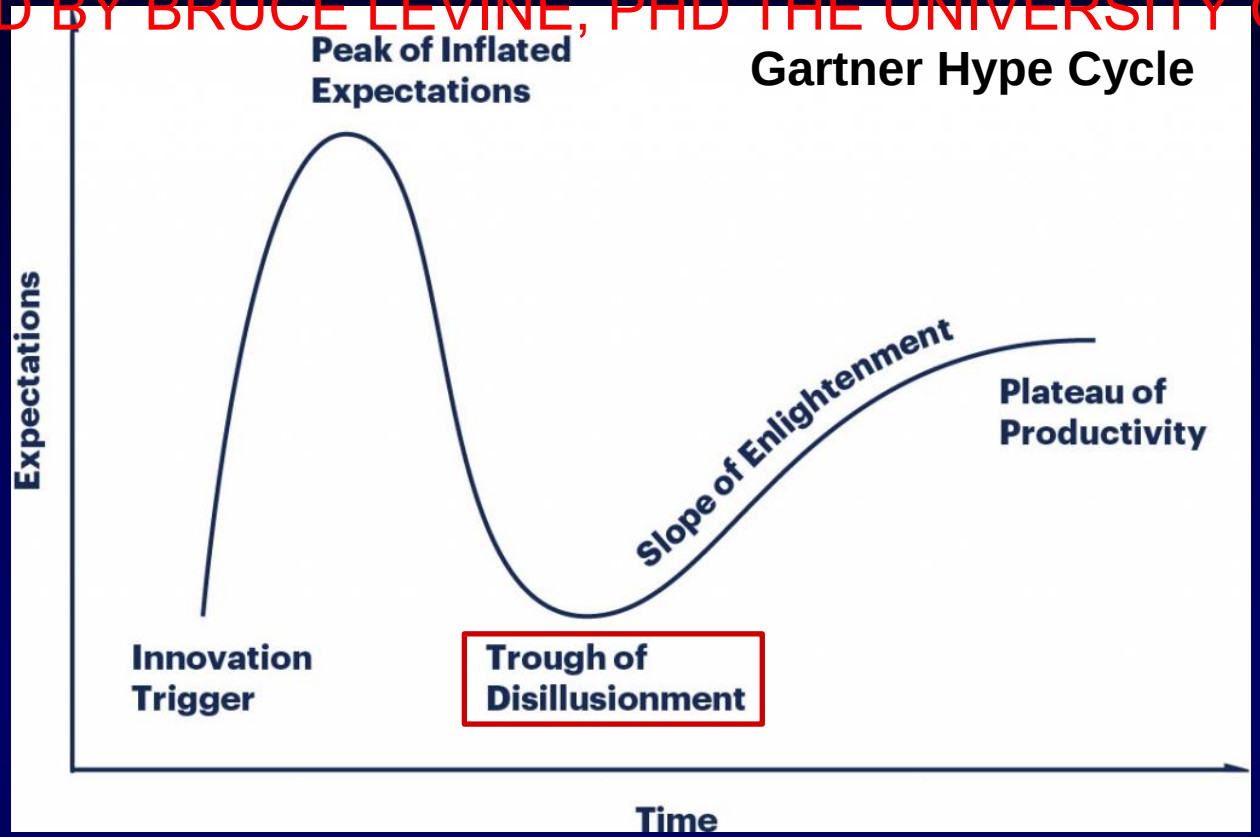


Prolonged survival and tissue trafficking following adoptive transfer of CD4ζ gene-modified autologous CD4+ and CD8+ T cells in human immunodeficiency virus–infected subjects

Ronald T. Mitsuyasu, Peter A. Anton, Steven G. Deeks, David T. Scadden, Elizabeth Connick, Matthew T. Downs, Andreas Bakker, Margo R. Roberts, Carl H. June, Sayeh Jalali, Andy A. Lin, Rukmini Pennathur-Das, and Kristen M. Hege

BLOOD, 1 AUGUST 2000 • VOLUME 96, NUMBER 3

CELL GENESYS



First clinical experiences in cancer:

Lamers et al. *J Clin Oncol*. 24:e20, 2006

Kershaw et al. *Clin Cancer Res*. 12: 6106, 2006

Park et al. *Mol Ther*. 15:825-833, 2007

Pule et al. *Nat Med*, 14:1264, 2008

> Trials disappointing due to poor T cell engraftment

2023

TECARTUS™
(brexucabtagene autoleucel) Suspension for IV infusion

Breyanzi

CARVYKTI

Abecma

KYMRIAH®
(tisagenlecleucel) Suspension for IV infusion

TILs (melanoma)
Netherlands
Lifileucel

TCR (Synovial Sarcoma)
Afami-cel

Engineered Stem Cells

zynteglo™
(autologous CD34+ cells encoding $\beta^{A\text{-}T87Q}$-globin gene)

skysona

libmeldy™
(atidarsagene autotemcel)

Allogeneic post HCT

EBVALLO®
tabelecleucel

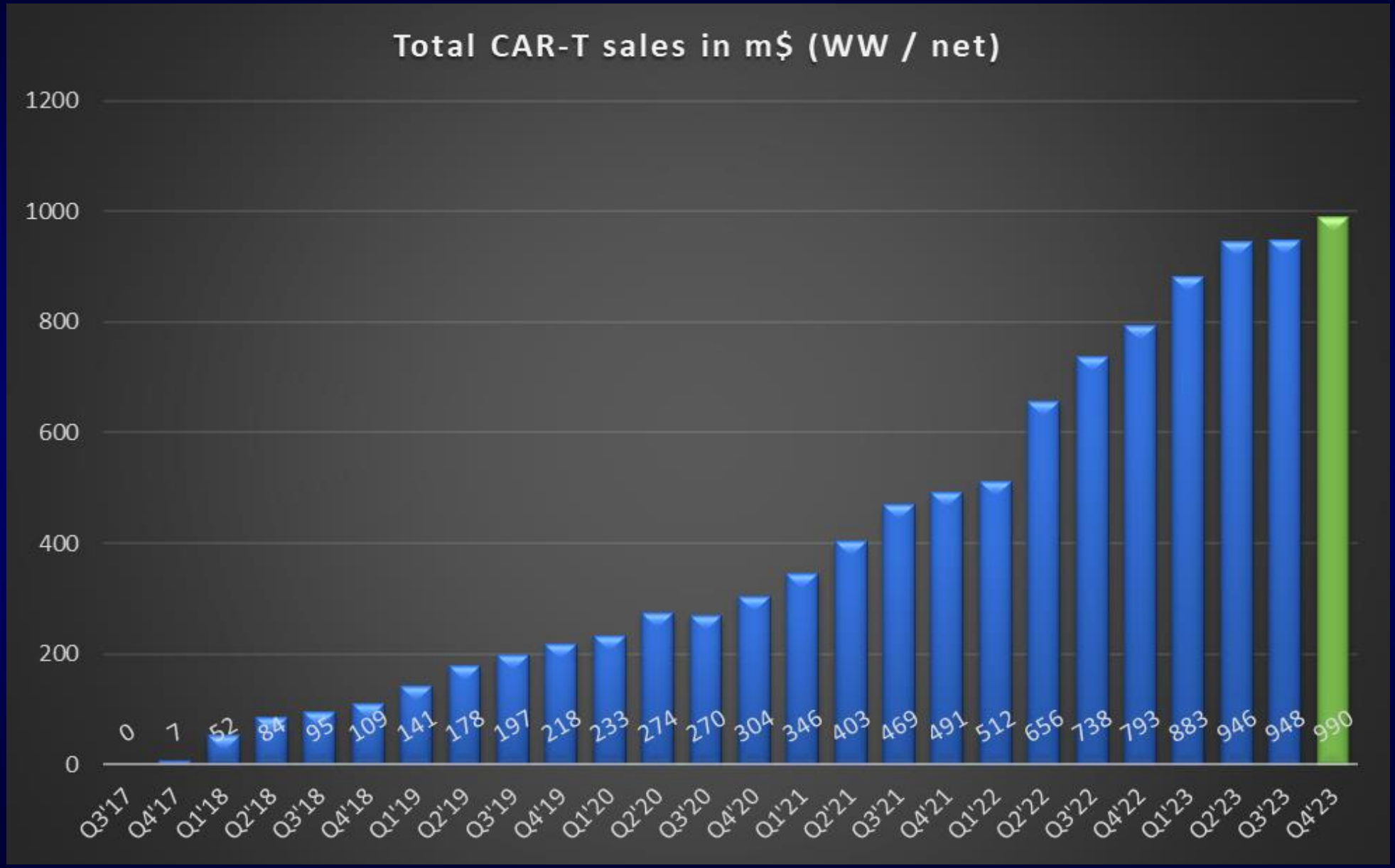
Sickle Cell Disease
Exa-cel (PDUFA 12/8)
Lovo-cel (PDUFA 12/20)

U.S. Approved Gene Therapies

- Kymriah (2017)
- Yescarta (2017)
- Luxturna (2017)
- Zolgensma (2019)
- Tecartus (2020)
- Breyanzi (2021)
- Abecma (2021)
- Carvykti (2022)
- Zynteglo (2022)
- Skysona (2022)
- Hemgenix (2022)
- Adstiladrin (2022)
- Vyjuvek (2023)
- Elevidys (2023)
- Roctavian (2023)

Stem cell T cell Directly administered

Global CAR T Sales (Millions $US by Q)



Credit: Bertrand Delsuc

RESEARCH ARTICLE

ADOPTIVE T CELL TRANSFER

HIV

Sci Transl Med 4, 132ra53 (2012)

Decade-Long Safety and Function of Retroviral-Modified Chimeric Antigen Receptor T Cells

John Scholler,[1]* Troy L. Brady,[2]* Gwendolyn Binder-Scholl,[1] Wei-Ting Hwang,[3] Gabriela Plesa,[1] Kristen M. Hege,[4] Ashley N. Vogel,[1] Michael Kalos,[1] James L. Riley,[2] Steven G. Deeks,[5] Ronald T. Mitsuyasu,[6] Wendy B. Bernstein,[7] Naomi E. Aronson,[7,8] Bruce L. Levine,[1] Frederic D. Bushman,[2†] Carl H. June[1†]

The success of adoptive T cell gene transfer for treatment of cancer and HIV is predicated on generating a response that is both durable and safe. We report long-term results from three clinical trials to evaluate gammaretroviral vector–engineered T cells for HIV. The vector encoded a chimeric antigen receptor (CAR) composed of CD4 linked to the CD3ζ signaling chain (CD4ζ). CAR T cells were detected in 98% of samples tested for at least 11 years after infusion at frequencies that exceeded average T cell levels after most vaccine approaches. The CD4ζ transgene retained expression and function. There was no evidence of vector-induced immortalization of cells; integration site distributions showed no evidence of persistent clonal expansion or enrichment for integration sites near genes implicated in growth control or transformation. The CD4ζ T cells had stable levels of engraftment, with decay half-lives that exceeded 16 years, in marked contrast to previous trials testing engineered T cells. These findings indicate that host immunosuppression before T cell transfer is not required to achieve long-term persistence of

Science Translational Medicine

AAAS

nature

Explore content · About the journal · Publish with us

Article

Decade-long leukaemia remissions with persistence of CD4$^+$ CAR T cells

https://doi.org/10.1038/s41586-021-04390-6

Received: 7 May 2021

Accepted: 29 December 2021

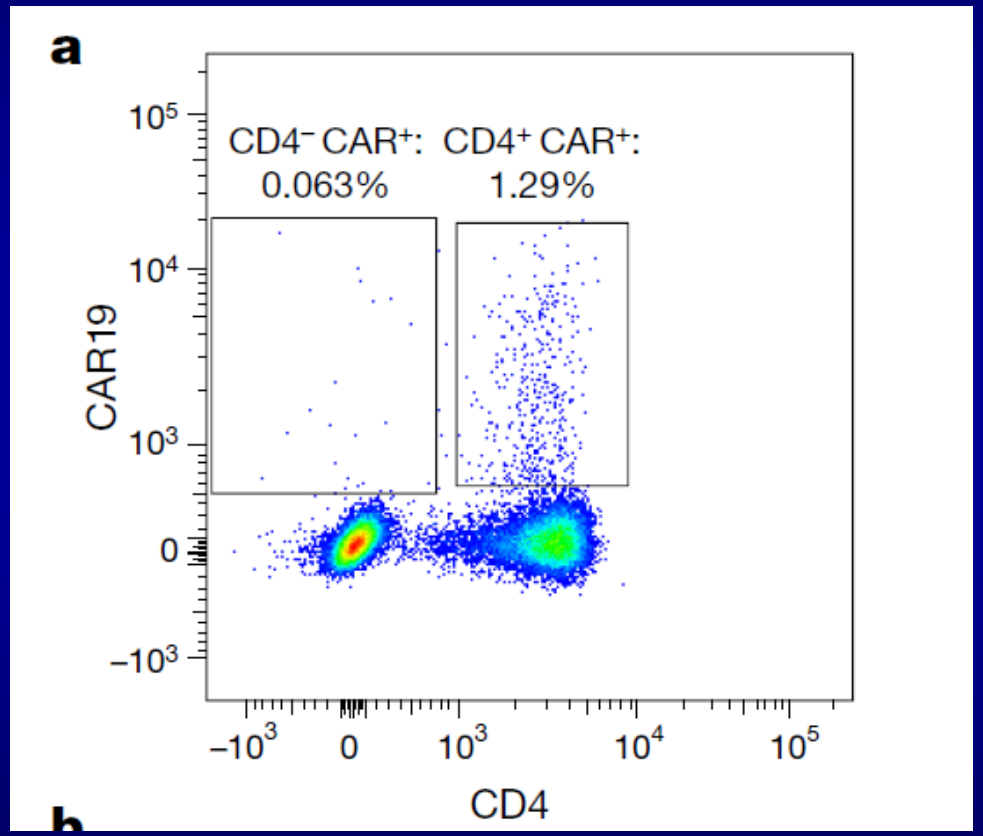
Published online: 02 February 2022

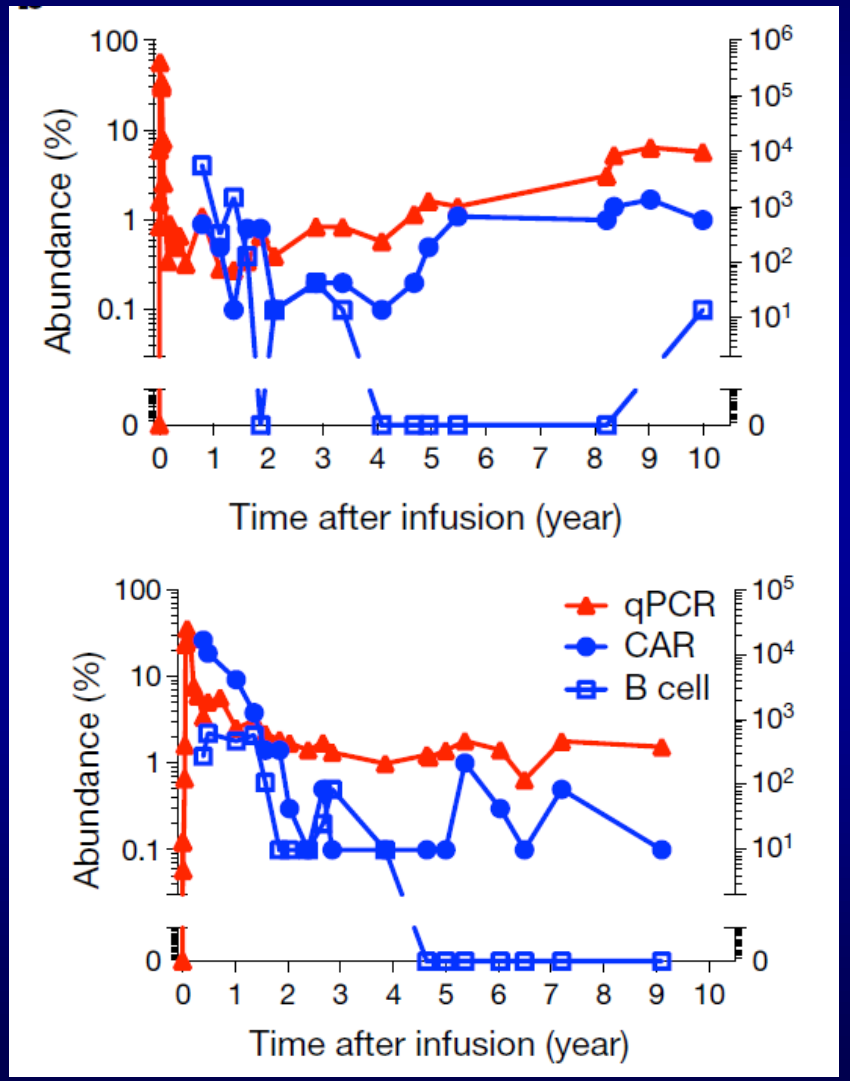
Check for updates

J. Joseph Melenhorst[1,2,3,4,5,15,16]✉, Gregory M. Chen[6,15], Meng Wang[1,2,3,14], David L. Porter[3,7,15], Changya Chen[8,9], McKensie A. Collins[1,2,3,10], Peng Gao[8,9], Shovik Bandyopadhyay[10], Hongxing Sun[1,2,3], Ziran Zhao[1,2,3], Stefan Lundh[1,2,3], Iulian Pruteanu-Malinici[11], Christopher L. Nobles[12], Sayantan Maji[1,2,3], Noelle V. Frey[3], Saar I. Gill[3], Lifeng Tian[1,3], Irina Kulikovskaya[1,2,3], Minnal Gupta[1,2,3], David E. Ambrose[1,2,3], Megan M. Davis[1,2,3], Joseph A. Fraietta[1,2,3,12], Jennifer L. Brogdon[11], Regina M. Young[1,2,3], Anne Chew[1,2,3], Bruce L. Levine[1,2,3], Donald L. Siegel[1,2,13], Cécile Alanio[4,5,14], E. John Wherry[4,5,14], Frederic D. Bushman[12], Simon F. Lacey[1,2,3], Kai Tan[2,4,6,9,10,16]✉ & Carl H. June[1,2,3,4,5,16]✉

The adoptive transfer of T lymphocytes reprogrammed to target tumour cells has demonstrated potential for treatment of various cancers[1–7]. However, little is known about the long-term potential and clonal stability of the infused cells. Here we studied long-lasting CD19-redirected chimeric antigen receptor (CAR) T cells in two patients with chronic lymphocytic leukaemia[1–4] who achieved a complete remission in 2010. CAR T cells remained detectable more than ten years after infusion, with sustained remission in both patients. Notably, a highly activated CD4$^+$ population emerged in

Tracking CAR T Cells For A Decade





Melenhorst, JJ et al. Nature. 2022 Feb;602(7897):503-509

Teach Every T Cell To Be All That It Can Be

Immunotherapy in Solid Tumors
The Challenges

- Antigen Escape
- Antigen Heterogeneity
- Trafficking
- Hostility of the tumor microenvironment

T Cell Quality/Potency Improvements

- Activators
- Cytokines
- Metabolism / transcriptional regulation
- Gene knockouts
- Which combinations?

Hotpot.ai

Data on Improving Cell Function Is Coming In Fast and Furiously

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER

Deleting DNMT3A in CAR T cells prevents exhaustion and enhances antitumor activity

Brooke Prinzing[1]†, Caitlin C. Zebley[1,2,3,4]†, Christopher T. Petersen[1]†‡, Yiping Fan[5], Alejandro Allo Anido[1], Zhongzhen Yi[1], Phuong Nguyen[1], Haley Houke[1], Matthew Bell[1,4], Dalia Haydar[1], Charmaine Brown[2], Shannon K. Boi[2], Shanta Alli[2], Jeremy Chase Crawford[2], Janice M. Riberdy[1], Jeoungeun J. Park[1], Sheng Zhou[1], Mireya Paulina Velasquez[1], Chris DeRenzo[1], Cicera R. Lazzarotto[6], Shengdar Q. Tsai[6], Peter Vogel[7], Shondra M. Pruett-Miller[8], Deanna M. Langfitt[1], Stephen Gottschalk[1]*, Ben Youngblood[2]*, Giedre Krenciute[1]*

Prinzing *et al.*, *Sci. Transl. Med.* **13**, eabh0272 (2021)
17 November 2021

JCI The Journal of Clinical Investigation

BET bromodomain protein inhibition reverses chimeric antigen receptor extinction and reinvigorates exhausted T cells in chronic lymphocytic leukemia

Weimin Kong, … , Golnaz Vahedi, Joseph A. Fraietta

J Clin Invest. 2021;131(16):1-16. https://doi.org/10.1172/JCI145459.

16 August 2021

Cell

Article

An NK-like CAR T cell transition in CAR T cell dysfunction

Charly R. Good, M. Angela Aznar, Shunichiro Kuramitsu, ..., Regina M. Young, Shelley L. Berger, Carl H. June

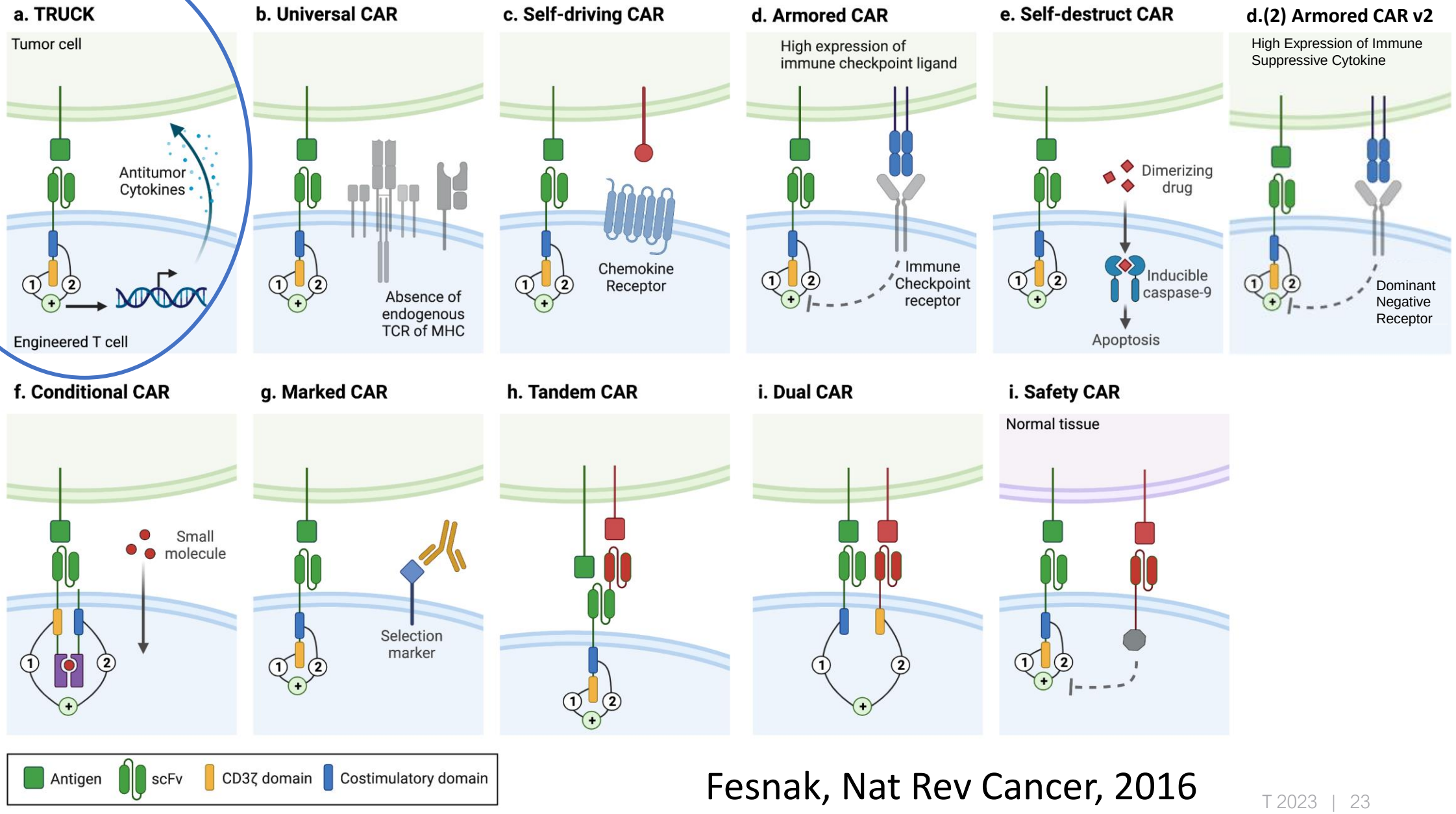
9 December 2021

- **Unlike WT CAR T cells, ID3 and SOX4 knockout CAR T cells retain anti-tumor immunity**

Dasatinib
Periodic stimulation
DNMT3a
IFN KO
IL-7/IL-15/IL-21
TWS119
SOCS3
ID3 SOX4
7SL
Anti-4-1BB
PD1 KO
TIGIT KO
TGFbDNR
CISH

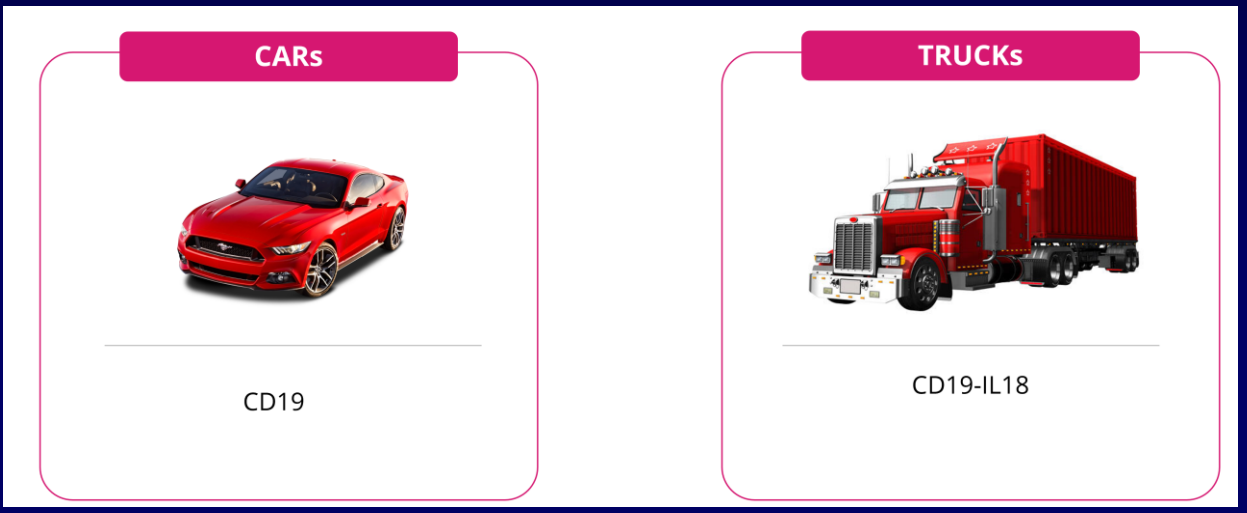
MICA/MICB
c-jun
CBL-B
BCL2L1 to upregulate BCL XL
PI3K inhibit. (e.g. bb21217)
Flt3L
TNFR2
PRODH2
Arginine
IL-18
RASA2 ablation
FOXO1
Lymphotoxin-β receptor
BLIMP1 and NR4A3

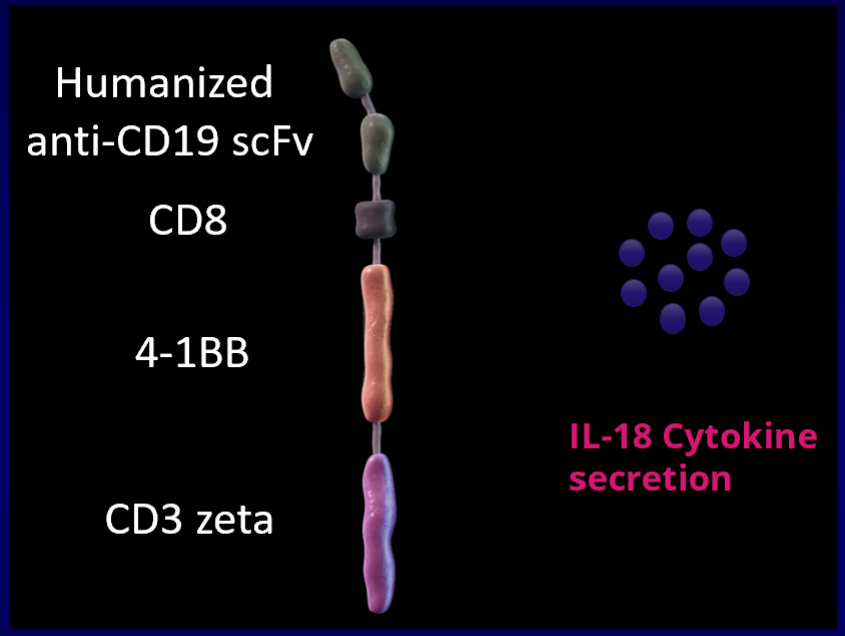
Next Generation CARs



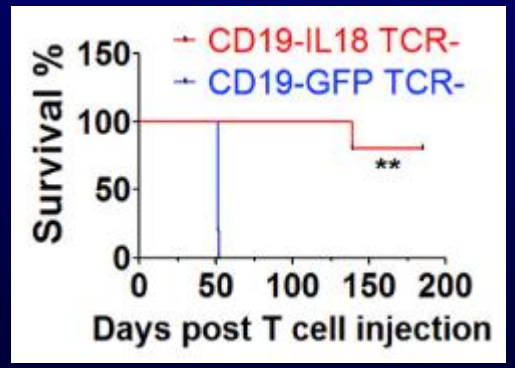
Fesnak, Nat Rev Cancer, 2016

TRUCKs = T cells redirected for antigen-unrestricted cytokine-initiated killing





Biliang Hu, PhD



Hu B, Ren J, Luo Y, Keith B, Young RM, Scholler J, Zhao Y, and June CH. Augmentation of Antitumor Immunity by Human and Mouse CAR T Cells Secreting IL-18. Cell reports. 2017; 20(13):3025-33.

Chmielewski M, and Abken H. CAR T Cells Releasing IL-18 Convert to T-Bet(high) FoxO1(low) Effectors that Exhibit Augmented Activity against Advanced Solid Tumors. *Cell reports.* 2017;21(11):3205-19.

Avanzi MP, Yeku O, Li X, Wijewarnasuriya DP, van Leeuwen DG, Cheung K, Park H, Purdon TJ, Daniyan AF, Spitzer MH, and Brentjens RJ. Engineered Tumor-Targeted T Cells Mediate Enhanced Anti-Tumor Efficacy Both Directly and through Activation of the Endogenous Immune System. *Cell reports.* 2018;23(7):2130-41.

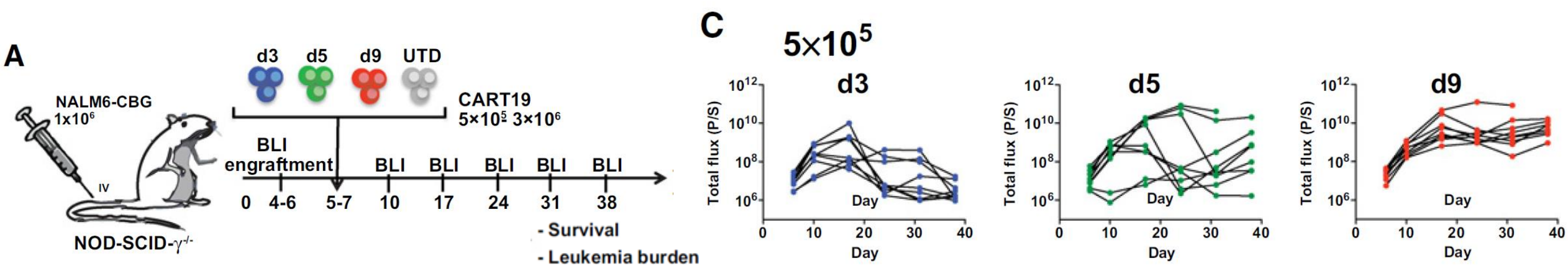
Manufacturing Improvements: Faster CAR's

Making Better and Cheaper CAR T

Research Article

Cancer Immunology Research Ghassemi et al, 2018

Reducing *Ex Vivo* Culture Improves the Antileukemic Activity of Chimeric Antigen Receptor (CAR) T Cells



Now Enrolling NCT04684563:

Phase I Trial of huCART19-IL18 Cells in Patients With R/R CD19+ NHL or CLL

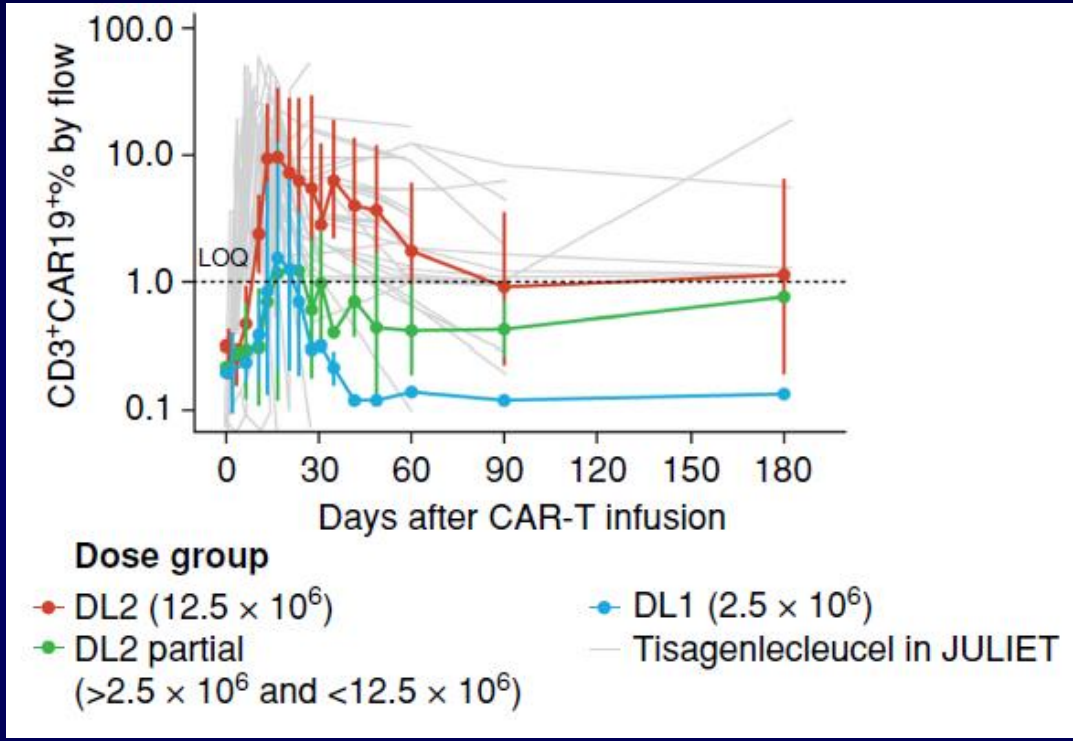
Contact: Abramson Cancer Center Clinical Trials Service 1-855-216-0098

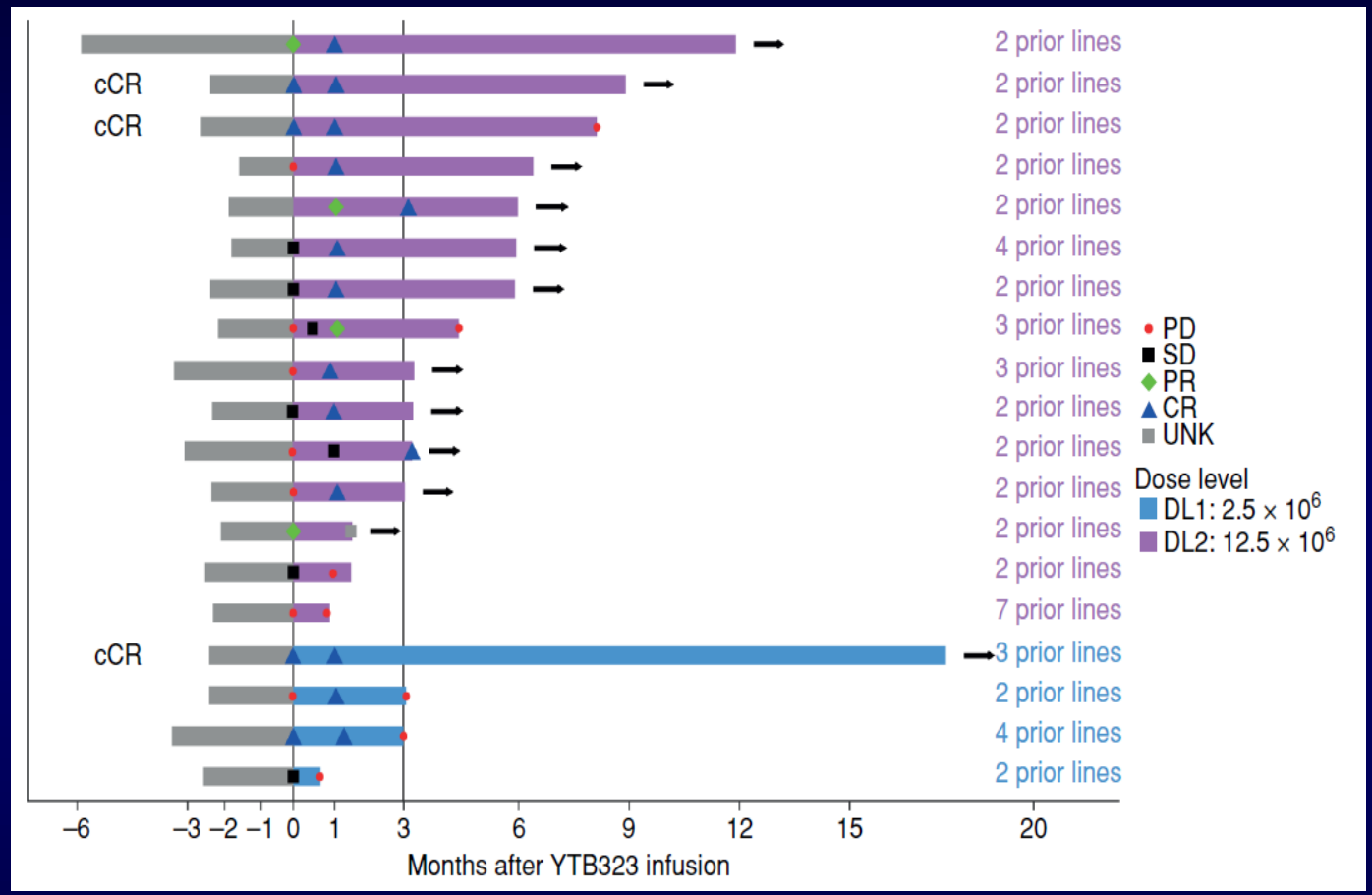
PennCancerTrials@emergingmed.com

Penn Medicine
Center for Cellular Immunotherapies

UNIVERSITY OF PENNSYLVANIA
Abramson Cancer Center

<2 Day Expansionless CAR T Cell Manufacturing

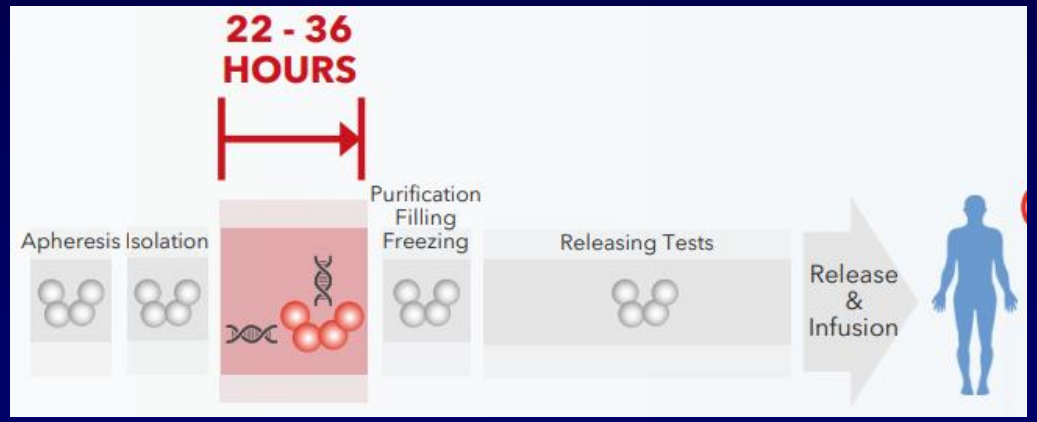


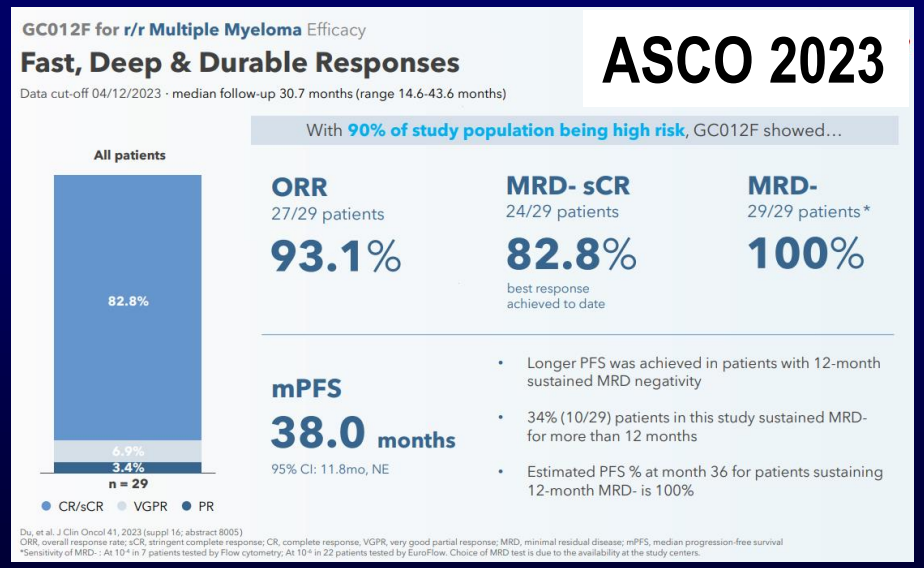


YTB323 favorable safety profile
demonstrated efficacy at DL1, DL2.
Comparable in vivo expansion to tisagen at 25X lower dose

Cancer Discov. 2023 Sep 6;13(9):1982-1997

24-Hours Manufacture of Anti-CD19/CD22 Dual CAR T Cells for Multiple Myeloma





RRMM patients with median 5 lines of therapy

nature biomedical engineering
ARTICLES
https://doi.org/10.1038/s41551-021-00842-6
Check for updates

Rapid manufacturing of non-activated potent CAR T cells

Saba Ghassemi[1,2], Joseph S. Durgin[1], Selene Nunez-Cruz[1,2], Jai Patel[1], John Leferovich[1,2], Marilia Pinzone[2], Feng Shen[1], Katherine D. Cummins[1], Gabriela Plesa[1], Vito Adrian Cantu[3], Shantan Reddy[3], Frederic D. Bushman[3], Saar I. Gill[1,4], Una O'Doherty[2], Roddy S. O'Connor[1,2] and Michael C. Milone[1,2]

Chimaeric antigen receptor (CAR) T cells can generate durable clinical responses in B-cell haematologic malignancies. The manufacturing of these T cells typically involves their activation, followed by viral transduction and expansion ex vivo for at least 6 days. However, the activation and expansion of CAR T cells leads to their progressive differentiation and the associated loss of anti-leukaemic activity. Here we show that functional CAR T cells can be generated within 24 hours from T cells derived

Quality Control Release Testing

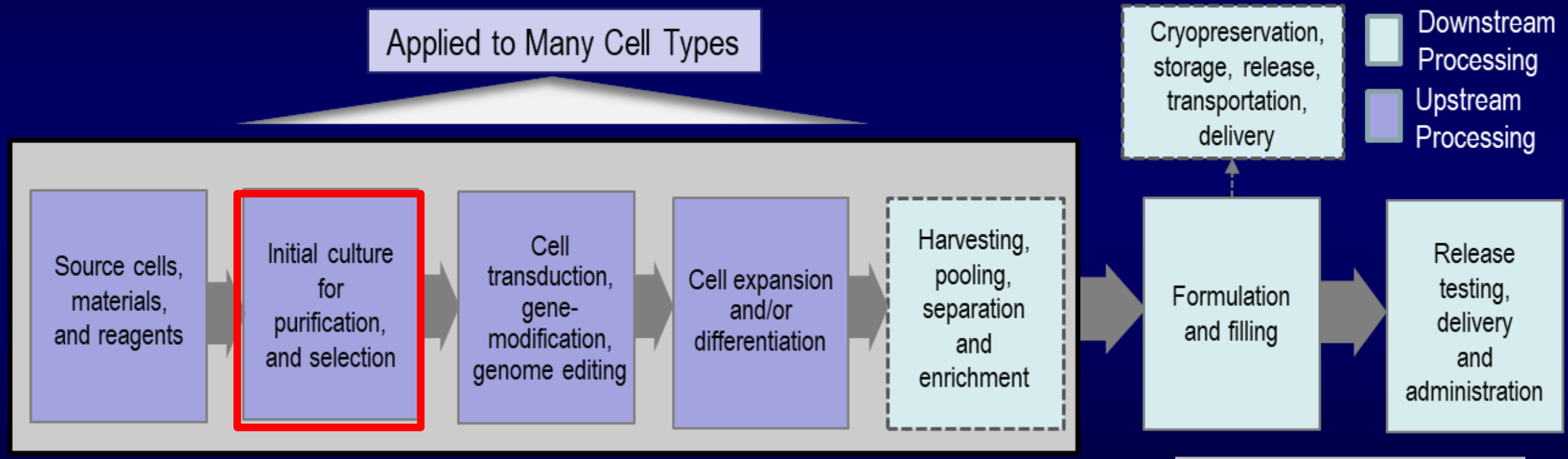
Conventional 9-10 Day Expanded CAR T

ASSAY	SITE	SPECIFICATION	RESULT
Cell Viability on Sentinel Vial	CVPF	≥ 70%	%
% CD3+CD45+		≥ 80%	%
Residual Bead Number		≤ 100 beads / 3x10⁶ cells	beads / 3x10⁶ cells
Endotoxin		≤ 3.5 EU/mL	EU/mL
Mycoplasma		Negative	
Transduction Efficiency (scFv Expression)		≥ 2%	%
Bactec Culture		No Growth at Day 7	at Day 7
Fungal Culture	HUP Microbiology	No Growth at day 7	at Day 7
Vector DNA Sequence (BBz PCR)	TCSL	≥0.02 – ≤4 Avg. copies per cell	Avg. copies/cell
VSV-G DNA (RCL)		< 50 Avg. copies VSV-G per µg DNA	Avg. copies / µg DNA

24 hr Non-Activated

- CAR expression?
- Vector copy number?
- RCL?
- Potency?

Ex Vivo Immune Cell Engineering Processing Flow



CMaT
NSF Engineering Research Center for Cell Manufacturing Technologies

Courtesy of Krish Roy

Not All Collections and Manufacturing Runs Are Predictable

Perfect is the Enemy of Good Enough

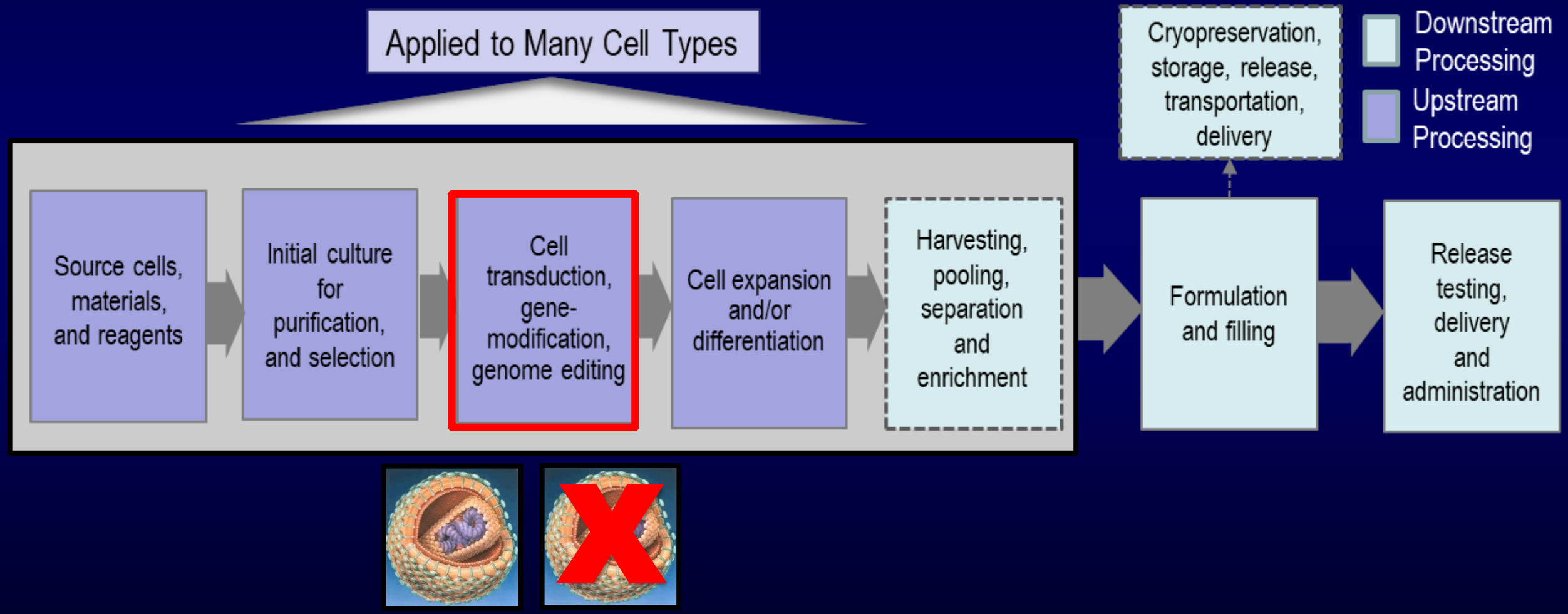
What is Good Enough?

CQA's of Raw Material

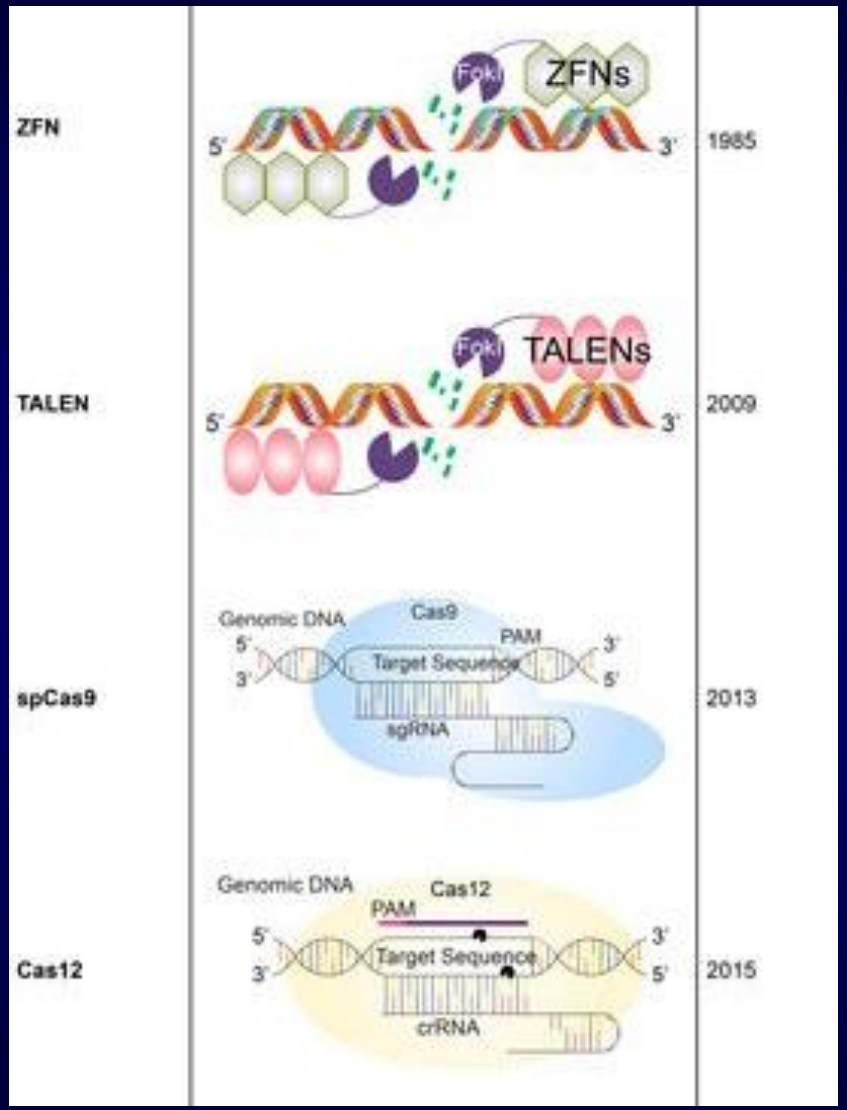
- How do you know you (always) have the right cells?
- What cellular raw material is acceptable?

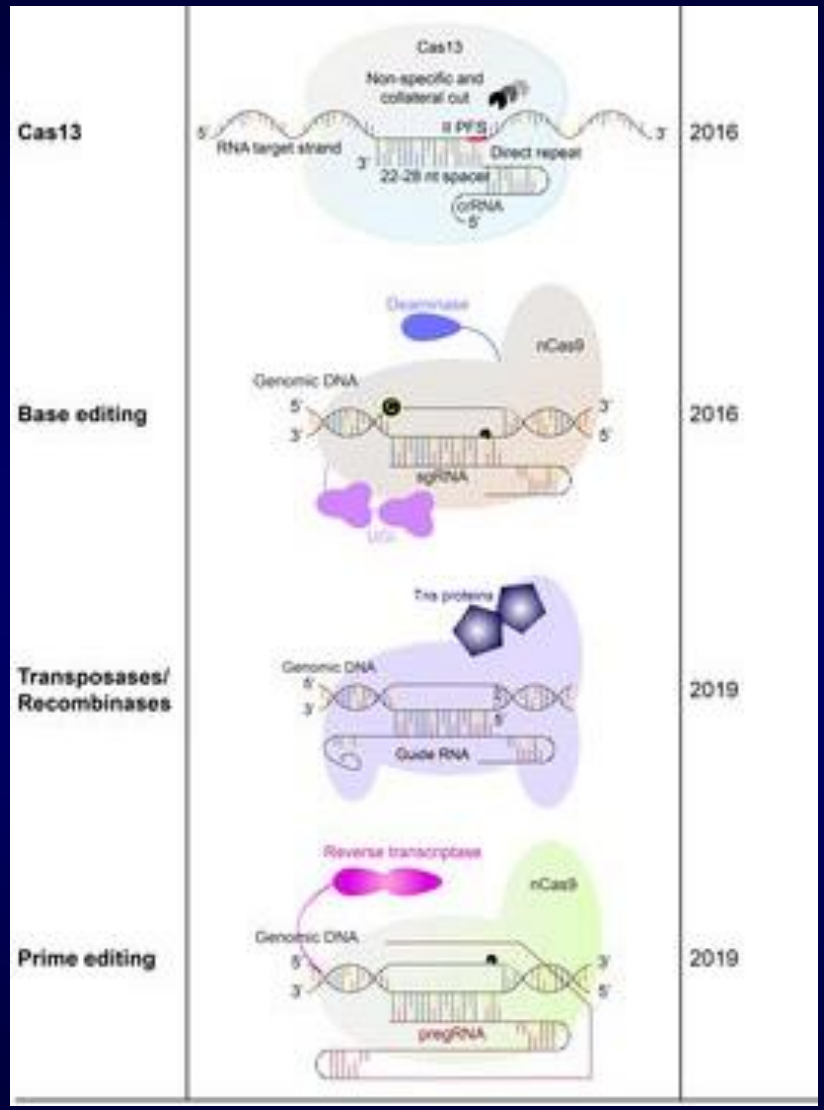
1) Are all of these colors blue?
2) Are all of these colors blue enough?
3) Do all of these colors have blue in them?

Activated T Cell Ex Vivo Processing Flow



Rapid Evolution of Gene Editing Tools





Epigenetic Editing?

New Technologies For Viral Free Cargo Delivery

What is important for Clinical Development?

- Efficiency
- Cargo Size
- Lack of toxicity
  - Gene disruption, metabolic disruption, viability
- Cell Yield
- Repeatability
- Regulatory compliance (DMF, 21 CFR Part 11)

CAR Cells Move Beyond Oncology

- CAR T Cells for HIV/AIDS

Multispecific anti-HIV duoCAR-T cells display broad in vitro antiviral activity and potent in vivo elimination of HIV-infected cells in a humanized mouse model

Kim Anthony-Gonda[1,*], Ariola Bardhi[2,*], Alex Ray[2], Nina Flerin[2], Mengyan Li[2], Weizao Chen[3], Christina Ochsenbauer[4], John C. Kappes[4,5], Winfried Krueger[1], Andrew Worden[1], Dina Schneider[1], Zhongyu Zhu[1], Rimas Orentas[1,†], Dimiter S. Dimitrov[6,‡], Harris Goldstein[2,‡] and Boro Dropulić[1,‡]

- CAR T Cells for Autoimmunity/Tolerance

nature medicine ARTICLES https://doi.org/10.1038/s41591-022-02017-5

Mackensen et al. September 15, 2022

Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus

- CAR T Cells for Heart Failure and Fibrosis

nature

Aghajanian et al. 2019

Targeting cardiac fibrosis with engineered T cells

- CAR T Cell for Aging?

Article

Senolytic CAR T cells reverse senescence-associated pathologies

Amor et al. Nature, 2020

T Cells Beyond CARs- TCRs and TILs

RESEARCH Lowery *et al.*, *Science* **375**, 877–884 (2022) 25 February 2022

CANCER IMMUNOLOGY

Molecular signatures of antitumor neoantigen-reactive T cells from metastatic human cancers

Frank J. Lowery[1]*†, Sri Krishna[1]*†, Rami Yossef[1], Neilesh B. Parikh[1], Praveen D. Chatani[1], Nikolaos Zacharakis[1], Maria R. Parkhurst[1], Noam Levin[1], Sivasish Sindiri[1], Abraham Sachs[1], Kyle J. Hitscherich[1], Zhiya Yu[1], Nolan R. Vale[1], Yong-Chen Lu[1], Zhili Zheng[1], Li Jia[2], Jared J. Gartner[1], Victoria K. Hill[1], Amy R. Copeland[1], Shirley K. Nah[1], Robert V. Masi[1], Billel Gasmi[1], Scott Kivitz[1], Biman C. Paria[1], Maria Florentin[1], Sanghyun P. Kim[1], Ken-ichi Hanada[1], Yong F. Li[1], Lien T. Ngo[1], Satyajit Ray[1], Mackenzie L. Shindorf[1], Shoshana T. Levi[1], Ryan Shepherd[3], Chris Toy[1], Anup Y. Parikh[1], Todd D. Prickett[1], Michael C. Kelly[4], Rachel Beyer[1], Stephanie L. Goff[1], James C. Yang[1], Paul F. Robbins[1], Steven A. Rosenberg[1]*

The accurate identification of antitumor T cell receptors (TCRs) represents a major challenge for the engineering of cell-based cancer immunotherapies. By mapping 55 neoantigen-specific TCR clonotypes (NeoTCRs) from 10 metastatic human tumors to their single-cell transcriptomes, we identified signatures of

The NEW ENGLAND JOURNAL of MEDICINE

N ENGL J MED 386;22 NEJM.ORG JUNE 2, 2022

BRIEF REPORT

Neoantigen T-Cell Receptor Gene Therapy in Pancreatic Cancer

Rom Leidner, M.D., Nelson Sanjuan Silva, B.S., Huayu Huang, M.S., David Sprott, B.S., Chunhong Zheng, Ph.D., Yi-Ping Shih, Ph.D., Amy Leung, B.S., Roxanne Payne, M.N., Kim Sutcliffe, B.S.N., Julie Cramer, M.A., Steven A. Rosenberg, M.D., Ph.D., Bernard A. Fox, Ph.D., Walter J. Urba, M.D., Ph.D., and Eric Tran, Ph.D.

Open access Original research

Journal for ImmunoTherapy of Cancer

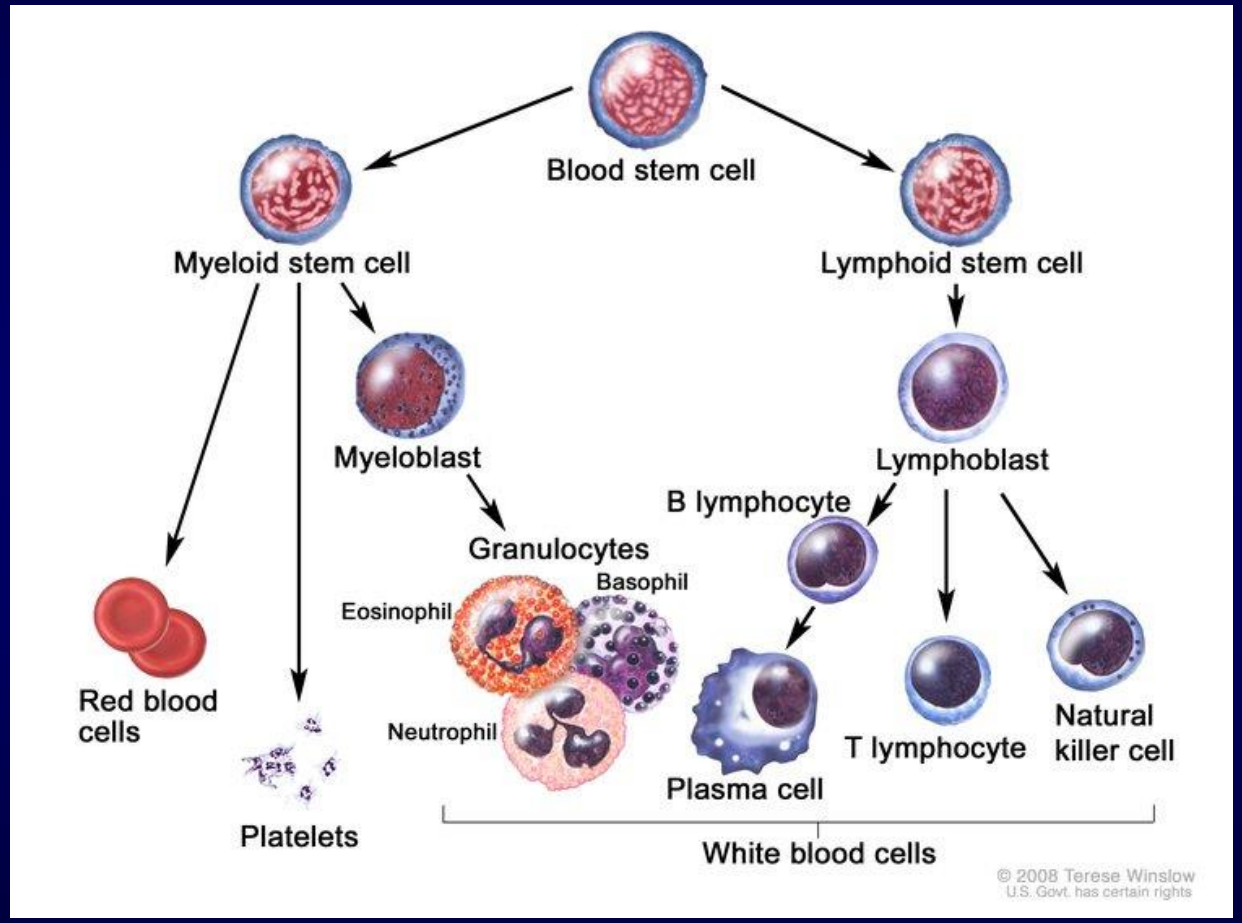
Phase I clinical trial evaluating the safety and efficacy of ADP-A2M10 SPEAR T cells in patients with MAGE-A10^{+} advanced non-small cell lung cancer

George R Blumenschein,[1] Siddhartha Devarakonda,[2] Melissa Johnson,[3] Victor Moreno,[4] Justin Gainor,[5] Martin J Edelman,[6] John V Heymach,[1] Ramaswamy Govindan,[2] Carlos Bachier,[7] Bernard Doger de Spéville,[4] Matthew J Frigault,[8] Anthony J Olszanski,[6] Vincent K Lam,[9] Natalie Hyland,[10] Jean-Marc Navenot,[11] Svetlana Fayngerts,[11] Zohar Wolchinsky,[10] Robyn Broad,[10] Dzmitry Batrakou,[10] Melissa M Pentony,[10] Joseph P Sanderson,[10] Andrew Gerry,[10] Diane Marks,[11] Jane Bai,[11] Tom Holdich,[10] Elliot Norry,[11] Paula M Fracasso [11]

Blumenschein GR, *et al. J Immunother Cancer* 2022;**10**:e003581. doi:10.1136/jitc-2021-003581

CAR Cells Move Beyond T Cells

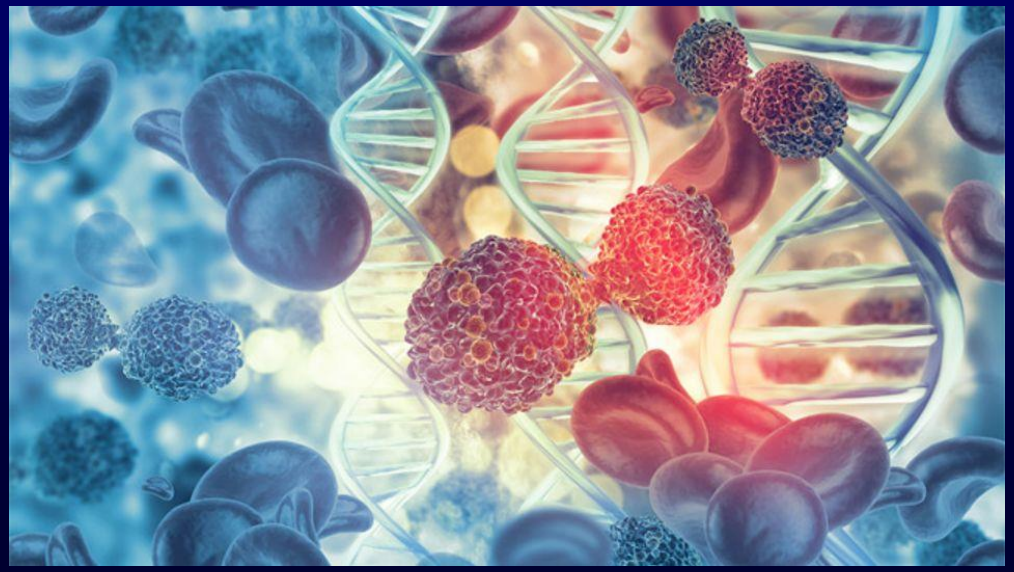
- CAR NK/iNK
- CAR macrophages
- CAR in blood stem cells
- CARs derived from iPSC



https://visualsonline.cancer.gov/details.cfm?imageid=7177

Future prospects

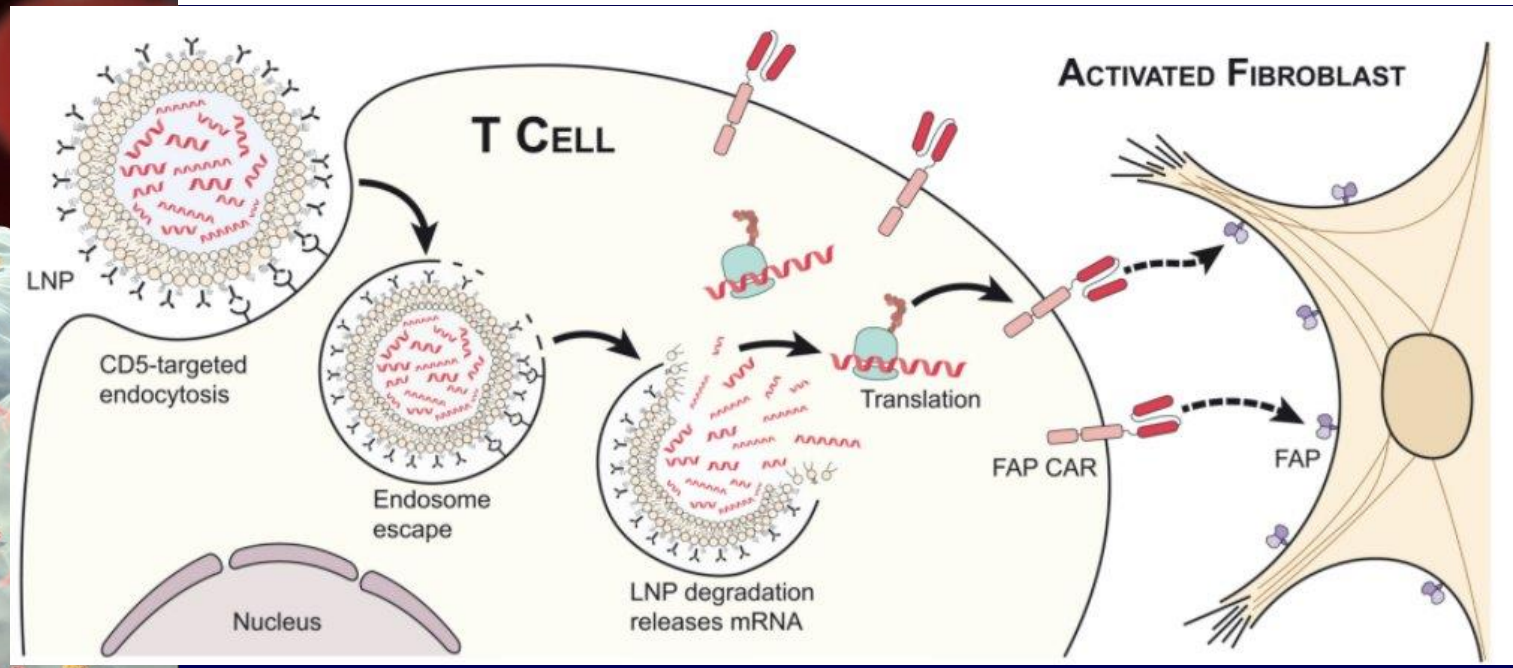
- Autologous?
- Off the shelf/allogeneic?
- Both? How is that possible?



CELL AND GENE THERAPY

CAR T cells produced in vivo to treat cardiac injury

Joel G. Rurik[1,2,3], István Tombácz[4]†, Amir Yadegari[4]†, Pedro O. Méndez Fernández[1,2,3], Swapnil V. Shewale[2], Li Li[1,2], Toru Kimura[4]‡, Ousamah Younoss Soliman[4], Tyler E. Papp[4], Ying K. Tam[5], Barbara L. Mui[5], Steven M. Albelda[4,6], Ellen Puré[7], Carl H. June[6], Haig Aghajanian[1,2,3]*, Drew Weissman[4]*, Hamideh Parhiz[4]*, Jonathan A. Epstein[1,2,3,4]*



Rurik et al.
Science 375, 91–96 (2022)
7 January 2022

Penn Medicine
University of Pennsylvania Health System

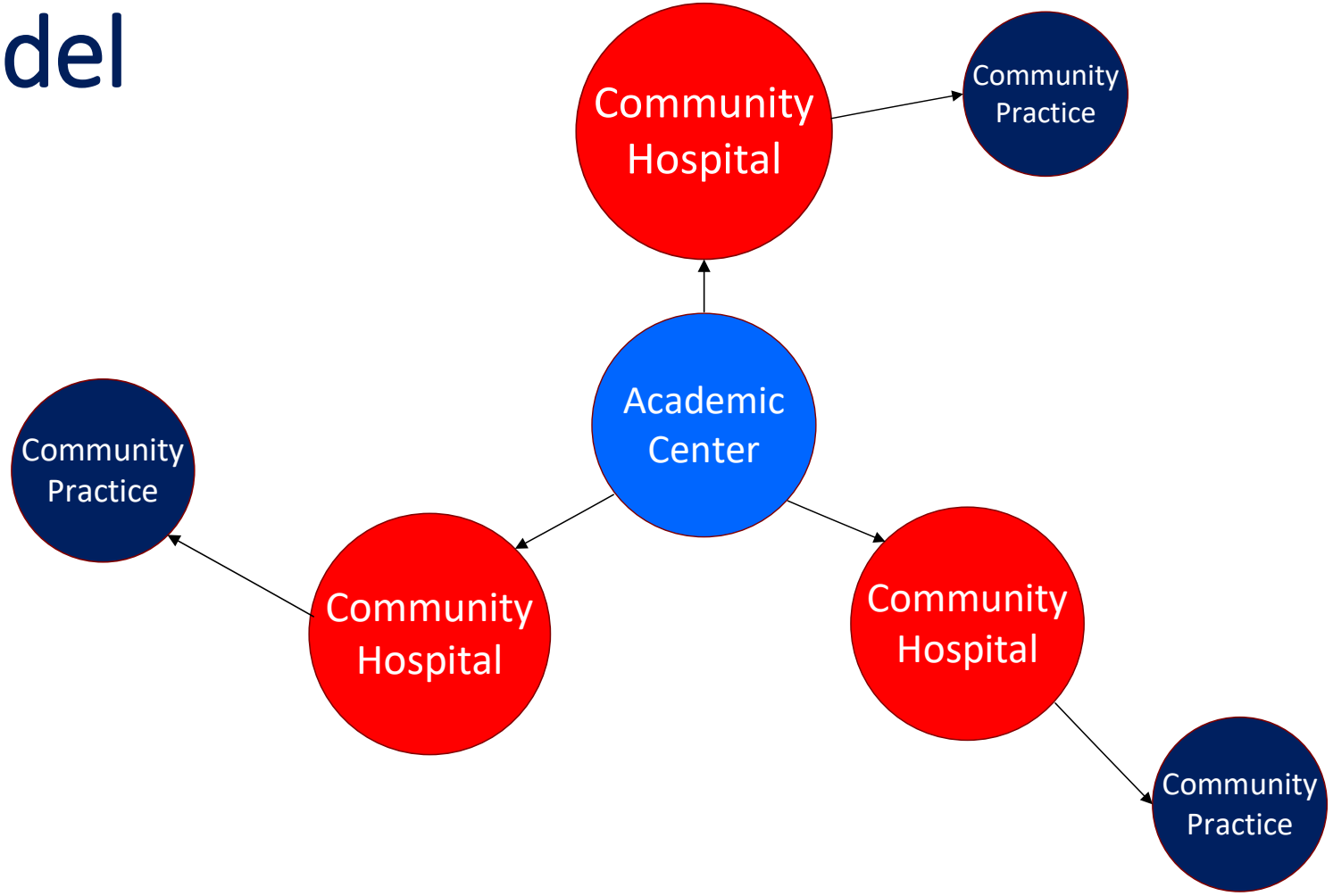
CELL THERAPY & TRANSPLANT

Penn Medicine: Developing Tools to Widen Patient Access to Complex Therapies

Hub and Spoke Model

Penn goal: To develop FACT accredited IEC sites at Penn community hospitals

- This model fosters continued growth of gene and cell therapy space to locations where access is undeveloped and allows academic to onboard next gen treatments
- Develops hospitals to manage toxicities consistent with REMS guidance from the FDA, keeping patients closer to home



Courtesy of Robert Richards, MS, MBA

Developing a Cell Therapy Infrastructure

Penn Presbyterian Medical Center

Chester County Hospital

Pharmaceutical Company

The Hospital of the University of Pennsylvania

Lancaster General Health

Pennsylvania Hospital

Princeton Health

Courtesy of Robert Richards, MS, MBA

Key Questions in Developing Cell Therapy Sites

1.) Standardization (Operations)

- How do you assure standardization of process/procedures but give autonomy to each site?

2.) Education

- How do standardize training of staff?

3.) Data

- How do you collect data to assure that new sites are performing at a high quality and have comparable outcomes to established transplant/cell therapy centers?

4.) Cost

- How do you develop a program at a site, at a low cost footprint, that likely has little or no resources for cell therapy?

Courtesy of Robert Richards, MS, MBA

Challenges in Delivering Cell Therapies to Patients

Research
& Development

Regulatory
Approval
&
Patient
Access

(Some) Critical Path Issues for Wider Patient Access

- Enhancing potency, especially for solid tumors
  - Armor, switches, combination therapies
- ex vivo Manufacturing complexity: cell-based living drugs, viral vectors
  - Automation/shortened ex vivo culture/shortened vein to vein
- Education & Training at all levels
  - ASTCT, ISCT, NMDP, et al.

(Some) Critical Path Issues for Wider Patient Access

- Enhancing potency, especially for solid tumors
  - Armor, switches, combination therapies
- ex vivo Manufacturing complexity: cell-based living drugs, viral vectors
  - Automation/shortened ex vivo culture/shortened vein to vein
- Education & Training at all levels
  - ASTCT, ISCT, NMDP, et al.
- Disparities: Geography, Race, Income, Caregiver
- Financial complexity/affordability
  - Predictive biomarkers
  - Value based payment links price to outcome

@BLLPHD

ACKNOWLEDGEMENTS

Penn Medicine
Center for Cellular Immunotherapies

UNIVERSITY OF PENNSYLVANIA
Abramson Cancer Center

Study Participants

FDA U.S. FOOD & DRUG ADMINISTRATION

The Leukemia & Lymphoma Society
Fighting Blood Cancers

ACGT National grants for cell and gene therapy cancer research
ALLIANCE FOR CANCER GENE THERAPY

PARKER INSTITUTE for CANCER IMMUNOTHERAPY

NIH National Institutes of Health
Turning Discovery Into Health

NOVARTIS

capstan therapeutics

TMUNITY™

@BLLPHD

It Takes A Village