Dana-Farber Cancer Institute

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

14° CONGRESO COLOMBIANO
20° CONGRESO IBEROAMERICANO
Cali, Valle del Cauca, Colombia
24 de abril de 2026

Perspectivas de las terapias celulares: pasado, presente y futuro

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Connell and O'Reilly Families
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Dept. of Medical Oncology
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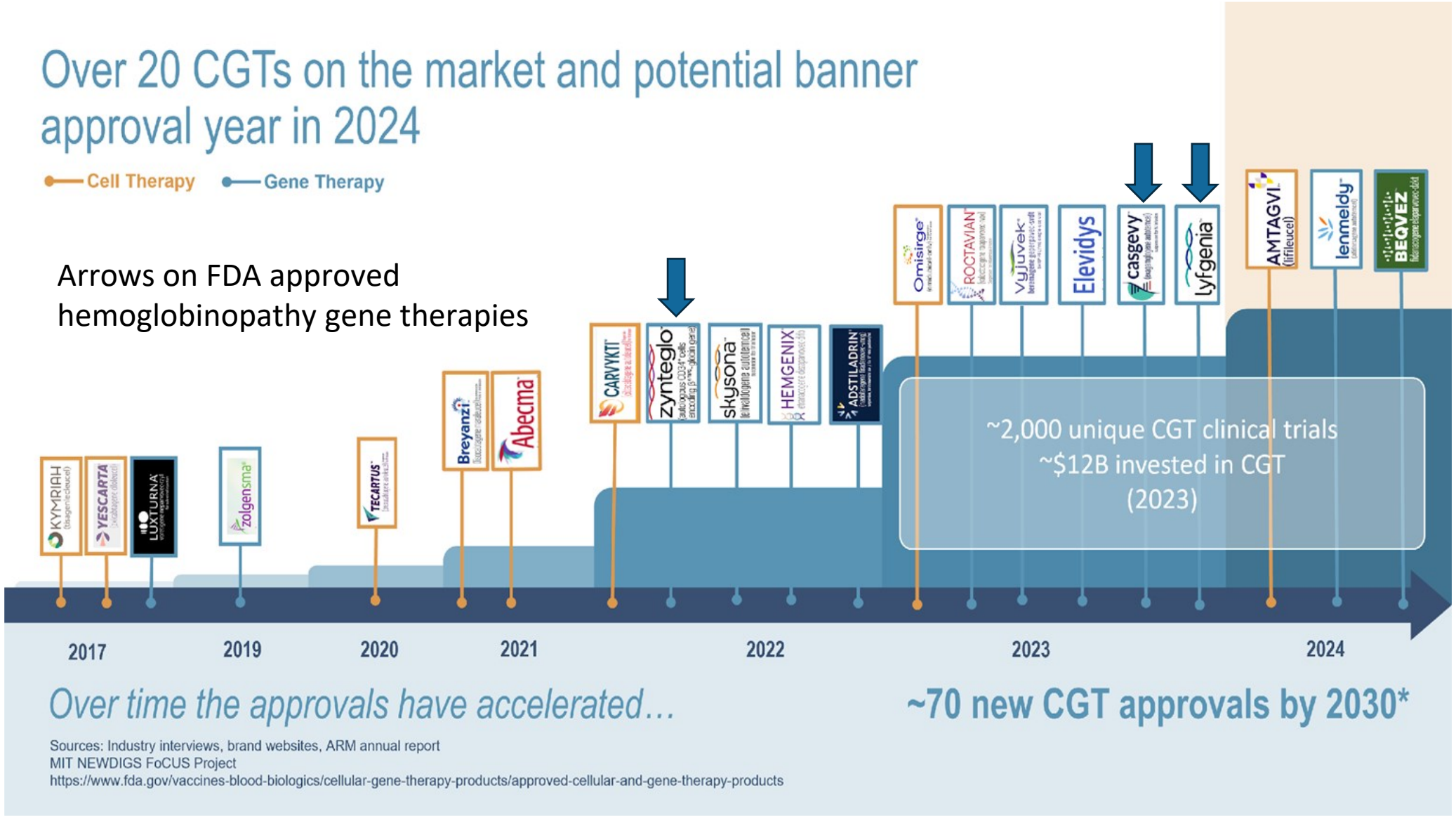
Association for the Advancement of Blood & Biotherapies

Disclosures

Jose A. Cancelas

- *AABB: President*
- *Teleflex: consultant*
- *Westat: contractor & grant support*
- *Velico Medical and HHS/BARDA: consultant and grant support*
- *Terumo BCT: grant support*
- Hemerus Medical LLC: grant support and consultant
- Hemanext: consultant
- Fresenius Kabi: consultant
- Rion: consultant
- Preservation Bio: consultant and share holder
- Platefuse: patent holder

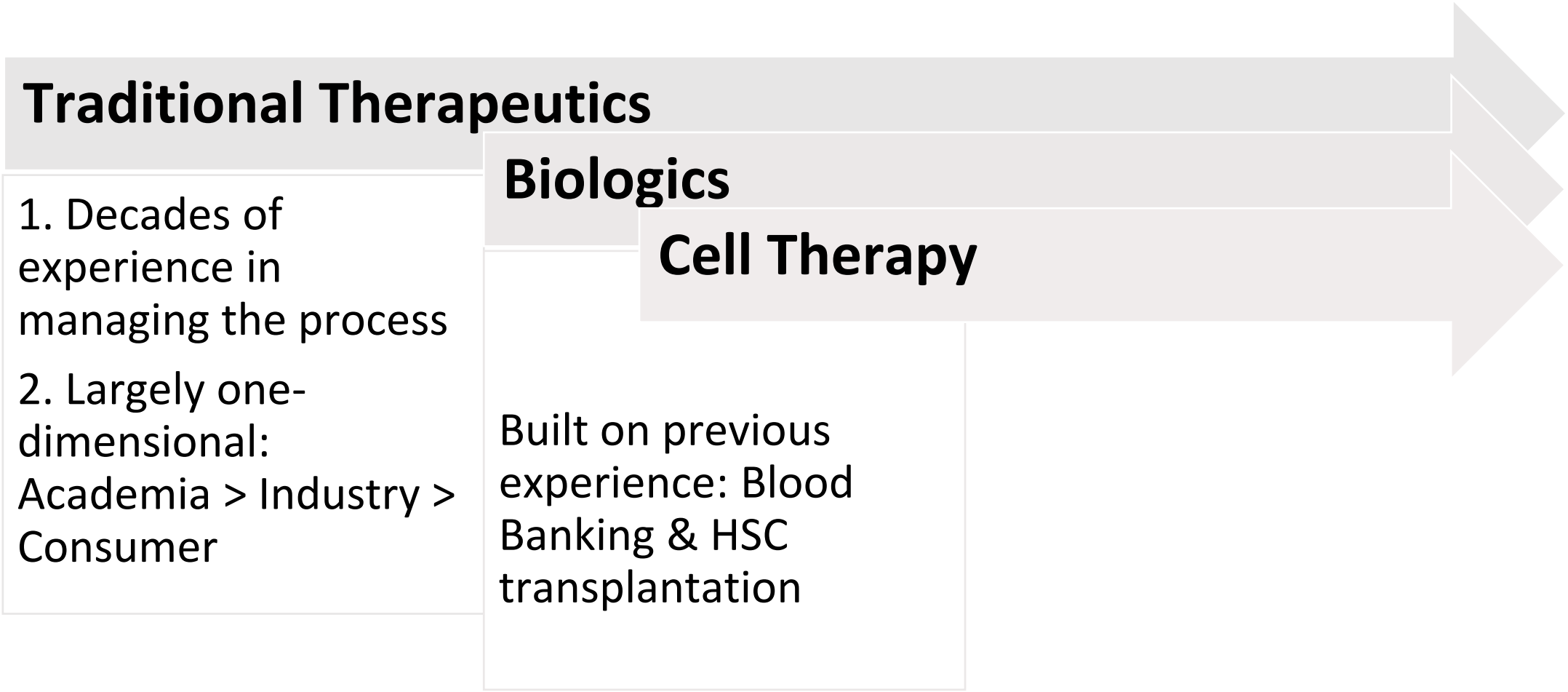
Over 20 CGTs on the market and potential banner approval year in 2024



Sources: Industry interviews, brand websites, ARM annual report
MIT NEWDIGS FoCUS Project
https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products

https://twolabs.com/cell-and-gene-therapy-pipeline-navigating-key-trends-and-pricing-dynamics/

Evolving Landscape of Development, Approval and Monitoring



Evolving Landscape of Development, Approval and Monitoring

Traditional Therapeutics

1. Decades of experience in managing the process
2. Largely one-dimensional: Academia / Industry > Patient

Biologics

Built on experier
Banking
transpla

Cell Therapy

1. Greater involvement of academic centers in the idea and development stage
2. Personalized, particularly autologous therapies
3. Treatment Center is the part of the manufacturing continuum
4. Issues related to long-term follow up

Current Trends in HSCGT/IEFGT/Vaccines/In vivo GT

- **Growing number of FDA licensed products (HSC, CAR-T, TILs)**
  - Multiple products in pipeline to be approved before the end of 2024 and many more in 2025.
  - Multiple investigational products in development
  - Challenge to define clinical priorities. Competition between “equals”.
  - Need of refined laboratory tests to demonstrate superiority.

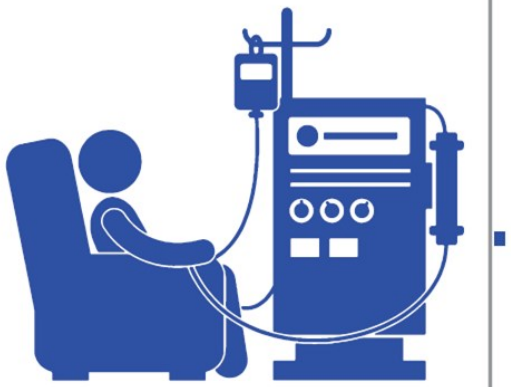
- **Increased use of investigational CTL, VSTs, MLNK, CAR-NK, B-cell, T-reg, iPSC-derived differentiated cells/tissues/organoids:** solid tumors, regenerative medicine, infectious diseases, autoimmune disorders,…

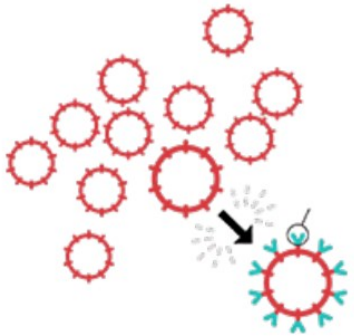
- **Gene Editing**
  - CRISPR/Cas9, base editors, prime editors
  - Concerns about long-term effects (potency and safety). Time will say!

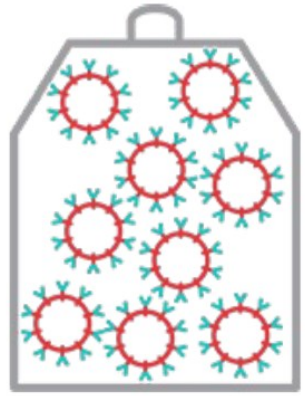
- **Personal Neoantigen Vaccines (TCR dependent or TCR independent)**
  - RNA-, DNA-, peptide- loaded nanoparticles
  - RNA-, DNA-, peptide- loaded cells

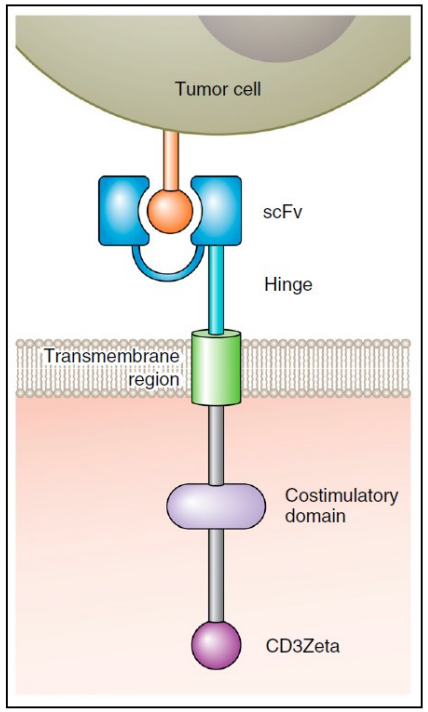
- **In vivo gene therapy**
  - Lentiviral vectors for CAR-T generation in vivo
  - Lentiviral vectors for SCD gene therapy

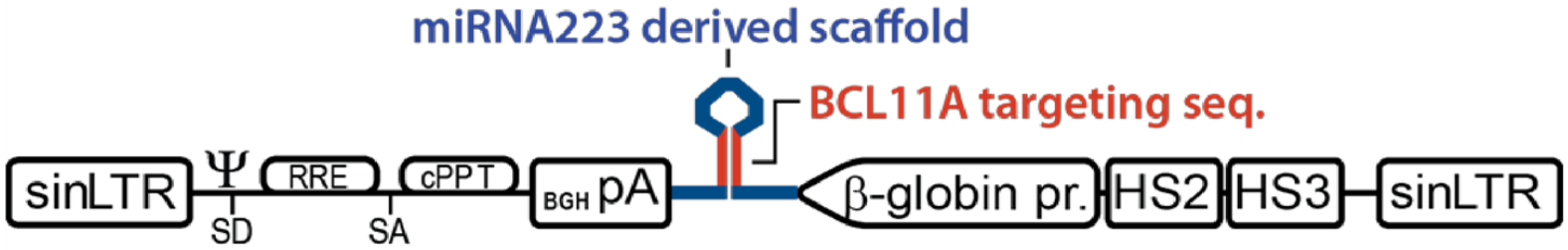
Currently licensed genetically modified T cell products





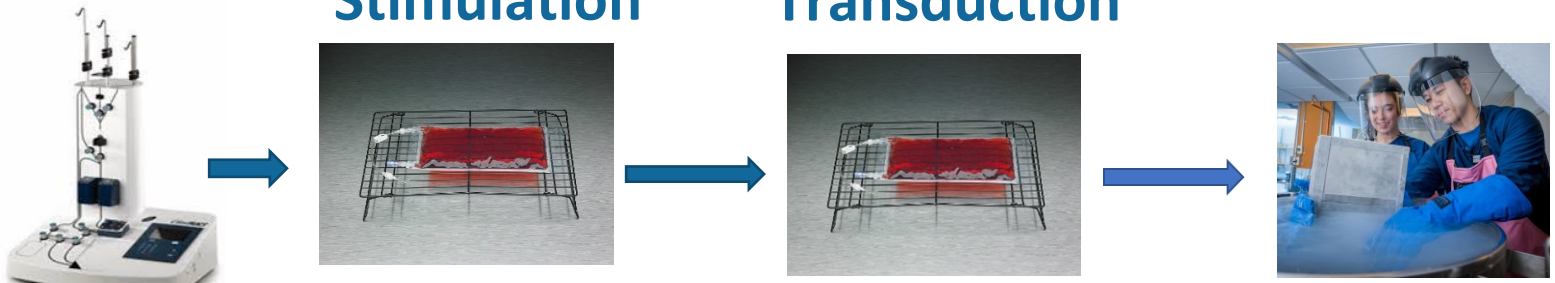






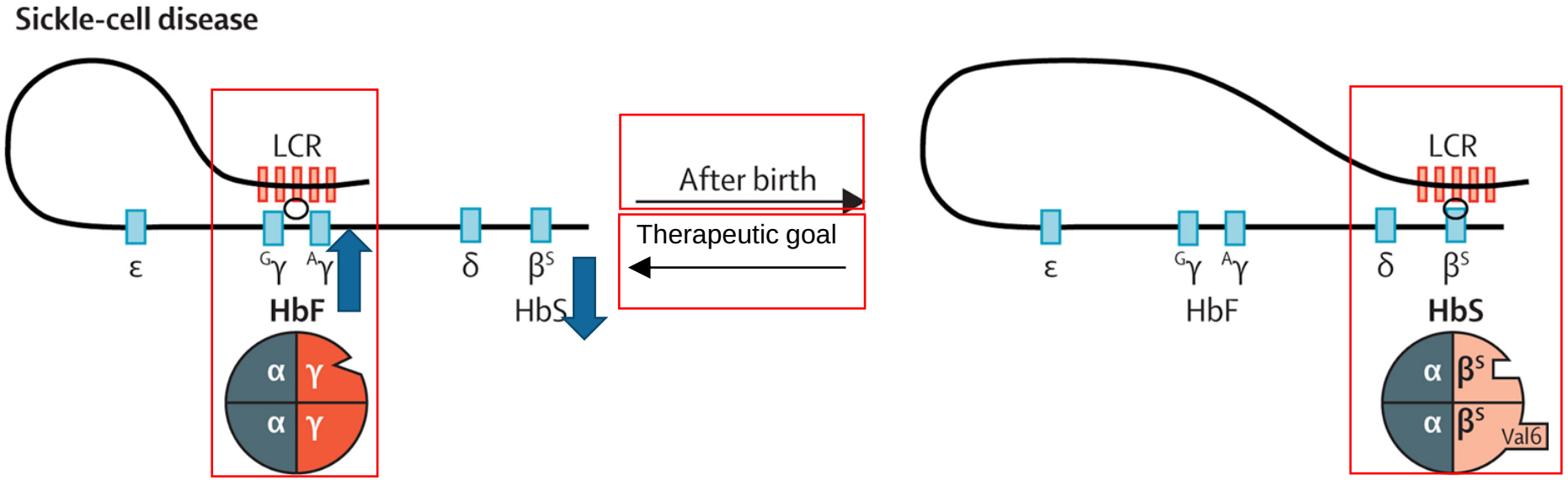
Pre-Stimulation

Transduction



Locus Control Region (LCR) repositions after birth to adult β-globin gene leading to SCD

Flipping the fetal to adult switch on SCD



Lettre and Bauer. Lancet, 2016

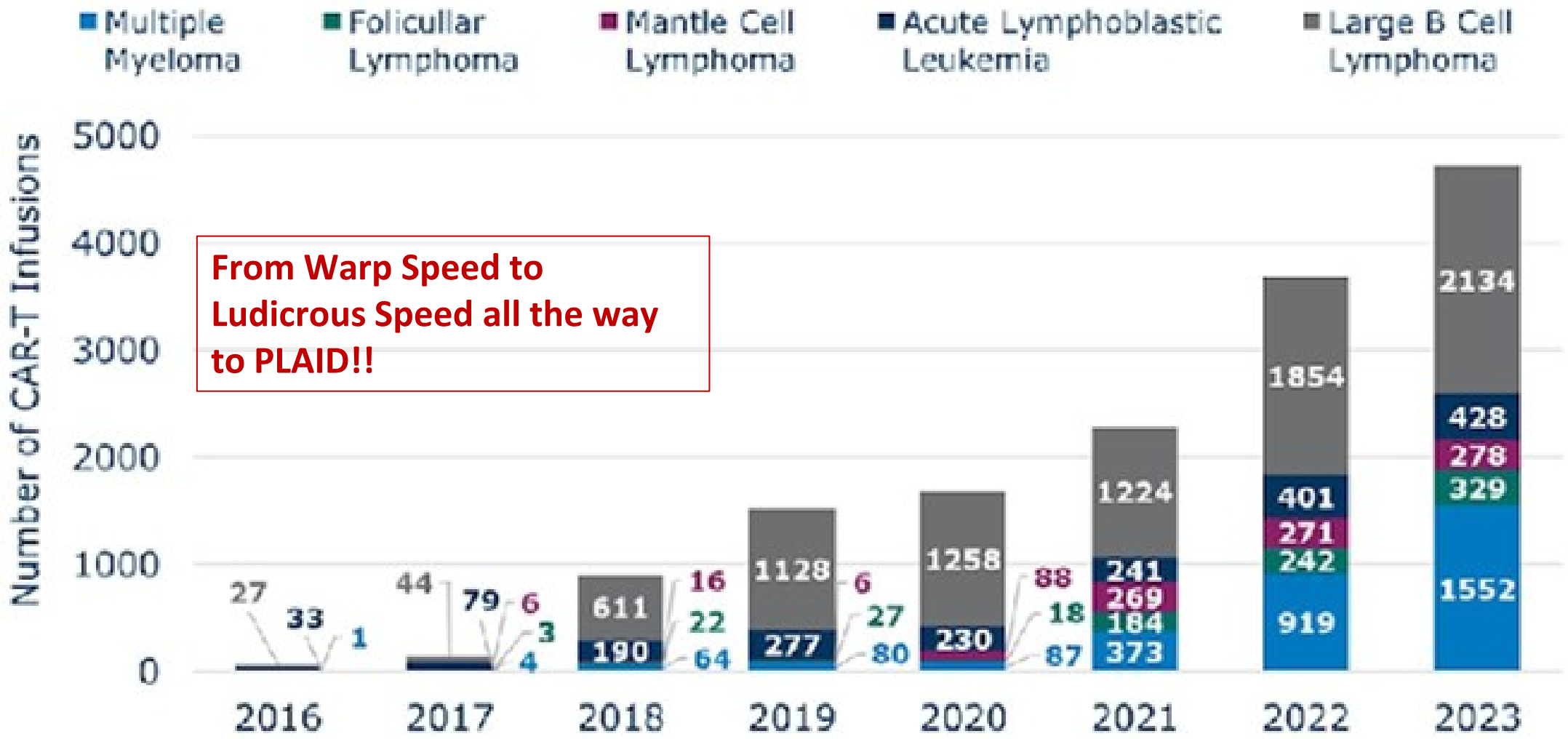
US FDA licensed cell-based therapeutics for specific indications: corporations

ABECMA (idecabtagene vicleucel)	BCMA CAR-T	Celgene Corporation, a BMS Company
AMTAGVI (lifileucel)	Melanoma TIL	Iovance Biotherapeutics, Inc.
AUCATZYL (obecabtagene autoleucel)	CD19 CAR-T	Autolus Limited
BREYANZI (lisocabtagene maraleucel)	CD19 CAR-T	Juno Therapeutics, Inc., a BMS Company
CARVYKTI (ciltacabtagene autoleucel)	BCMA CAR-T	Janssen Biotech, Inc.
CASGEVY (exagamglogene autotemcel [exa-cel])	GE: Sickle Cell Disease	Vertex Pharmaceuticals Incorporated
KYMRIAH (tisagenlecleucel)	CD19 CAR-T	Novartis Pharmaceuticals Corporation
LANTIDRA (donislecel)	Allogeneic pancreatic islets	CellTrans Inc.
LAVIV (Azficel-T)	Allogeneic fibroblasts (for nasolabial wrinkles)	Fibrocell Technologies
LENMELDY (atidarsagene autotemcel)	LVV: Metachromatic Leukodystrophy	Orchard Therapeutics (Europe) Limited
LYFGENIA (lovotibeglogene autotemcel [lovo-cel])	LVV: Sickle Cell Disease	bluebird bio, Inc.
OMISIRGE (omidubicel-onlv)	Nicotinamide-modified HPC(CB) - HSCT	Gamida Cell Ltd.
PROVENGE (sipuleucel-T)	Activated CD54+ PB cells – Prostate Ca.	Dendreon Corp.
REGENECYTE (HPC, Cord Blood)	Allo, unrelated HPC(CB)	StemCyte, Inc.
RETHYMIC	Allogeneic thymic tissue	Enzyvant Therapeutics GmbH
RYONCIL (remestemcel-L-rknd)	Allogeneic BM MSC - GvHD	Mesoblast, Inc.
SKYSONA (elivaldogene autotemcel)	LVV: Adrenoleukodistrophy	bluebird bio, Inc.
STRATAGRAFT	Allogeneic cultured keratynocytes/dermal fibroblasts in murine collagen	Stratatech Corporation
TECARTUS (brexucabtagene autoleucel)	CD19 CAR-T	Kite Pharma, Inc.
TECELRA (afamitresgene autoleucel)	MAGE4 TCR restricted engineered T-cell	Adaptimmune LLC
YESCARTA (axicabtagene ciloleucel)	CD19 CAR-T	Kite Pharma, Incorporated
ZYNTEGLO (betibeglogene autotemcel)	LVV: Beta-thalassemia	bluebird bio, Inc.

FDA approved CAR T cell products

Disease	CAR T-Cell Therapy Approved	5 Companies	Date of Approval	Target
Large B-Cell Lymphoma	Axicabtagene ciloleucel Tisagenlecleucel Lisocabtagene maraleucel	Kite NVS BMS	October 2017 May 2018 Feb 2021	CD19 CD19 CD19
Mantle Cell Lymphoma	Brexucabtagene autoleucel	Kite	July 2020	CD19
Follicular Lymphoma	Axicabtagene ciloleucel Tisagenlecleucel	Kite NVS	March 2021 May 2022	CD19 CD19
Chronic Lymphocytic Leukemia	Lisocabtagene maraleucel	BMS	March 2024	CD19
Multiple Myeloma	Idecabtagene vicleucel Ciltacabtagene autoleucel	BMS Janssen	March 2021 Feb 2022	BCMA BCMA
Adult ALL	Brexucabtagene autoleucel Obecabtagene Autoleucel	Kite Autolus	October 2021 November 2024	CD19 CD19
Pediatric ALL	Tisagenlecleucel	NVS	August 2017	CD19

Number of CAR-T Infusions by Indication in the US Annually

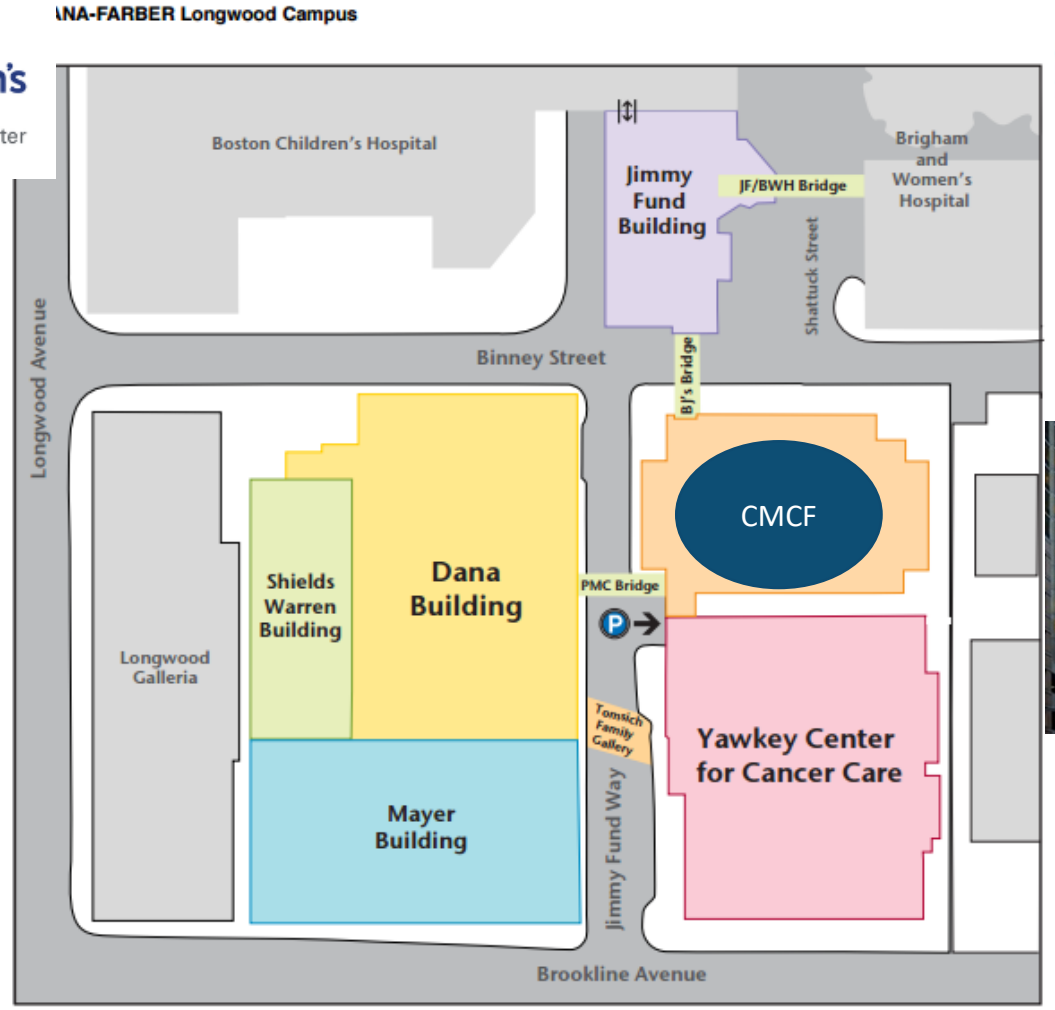


CMCF as an example of central, academic cell therapy focused facility

Dana-Farber Cancer Institute | Boston Children's

Dana-Farber/Boston Children's Cancer and Blood Disorders Center

BCH Pedi BMT/IEC



Dana-Farber Cancer Institute | Brigham Cancer Center

DF/BWH & DF Adult In-Pt

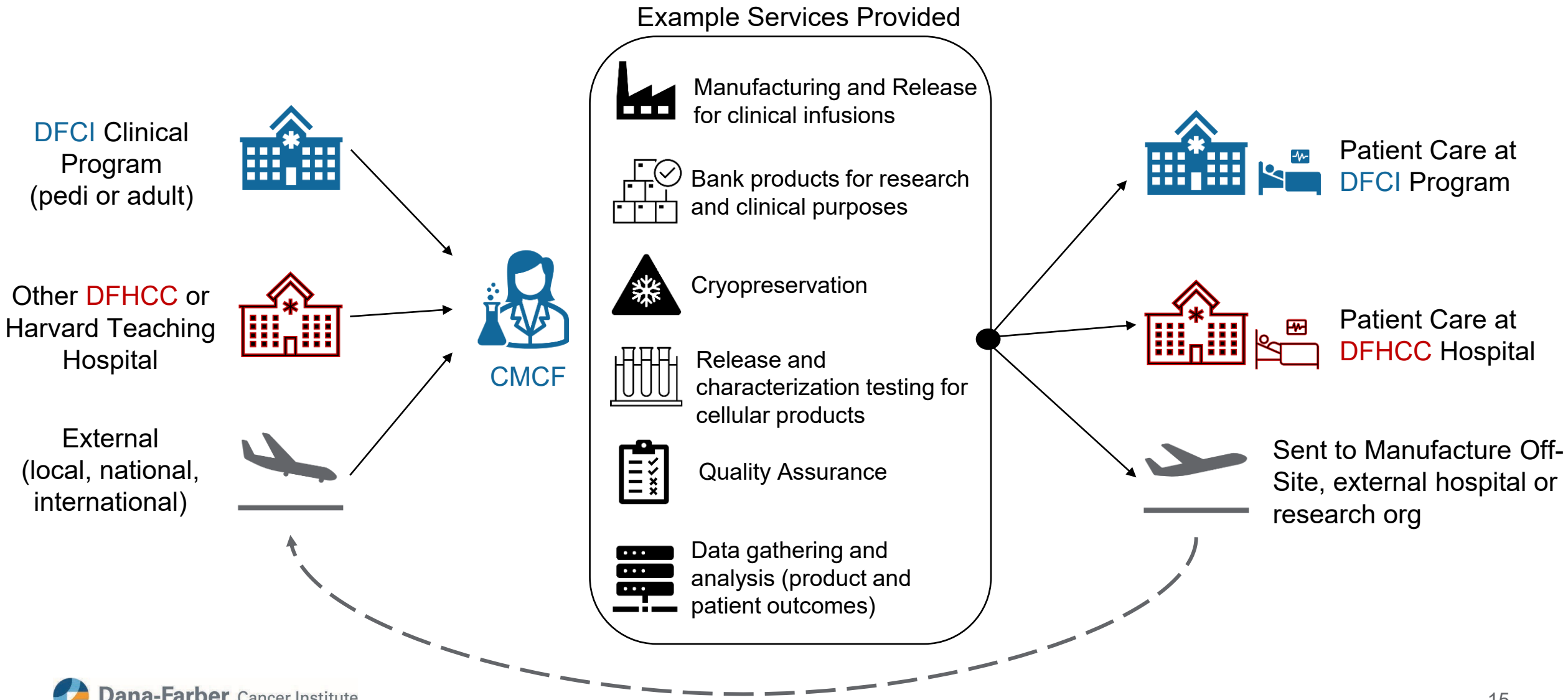
Dana-Farber Cancer Institute

DF Adult & Pedi Out-Pt

Connell and O'Reilly Families Cell Manipulation Core Facility (CMCF)

- **Supports Adult and Pediatric Stem Cell Transplant Programs at DFCI, BCH and BWH**
  - FACT Accredited cell manufacturing for minimal and extensive cell processing
- **Cell Pharmacy**
  - Support inventory management and distribution of FDA-approved and investigational cellular products manufactured at other facilities
- **Cell manufacturing support for clinical trials – Dana-Farber/Harvard Cancer Center BCH, BWH, MGH and other sites**
  - Hematopoietic stem cell transplantation – stem cell graft engineering
  - Cell therapy for cancer - CAR T cells, NK cells
  - Genetic modification of hematopoietic stem cells – gene therapy for sickle cell disease
  - Development of novel cell therapeutics
- **Work with basic and clinical investigators to develop novel cell therapies**
  - Technical
    - Scale up cell manufacturing, standardization of procedures
    - Reagents, equipment, quality control, release testing
    - Validation of manufacturing procedures for cellular products
  - Regulatory
    - Supports FDA Investigational New Drug (IND) applications

High-Level Schema of Clinical-Based Activity in CMCF



Examples of investigational products generated in an academic facility

Cell-based CGT & our academic experience

CAR-T (RVV/LVV)
T-reg (isolated or expanded)
TIL (unmod or RNA modified)
Vaccines (RNA or peptide)

VST (CMV, EBV, Adeno, BKV)

B-cells
CIML-NK
CAR-NK
CAR-M

MSC
iPSC/ Dopaminergic neurons
CALEC

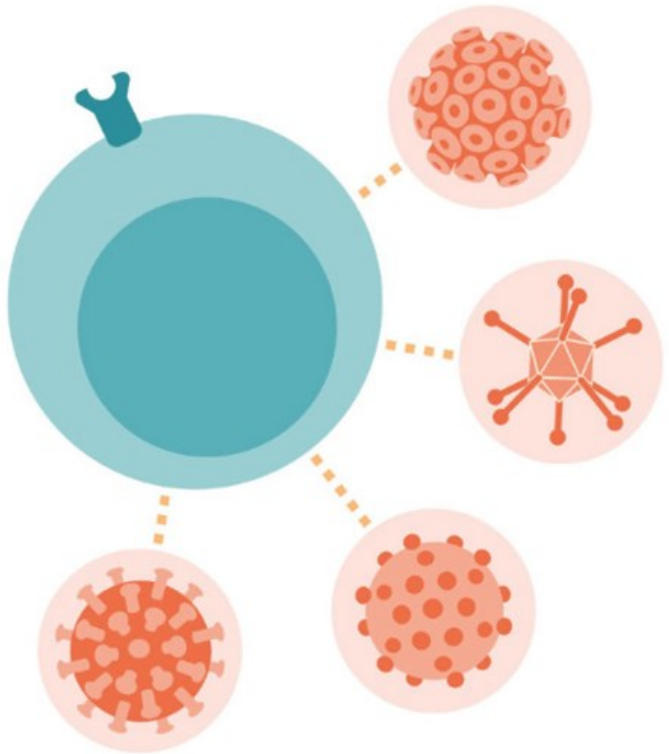
HSC, macrophages, neutrophils:
LVV
Gene editing

Master Cell Banks for viral production
Master Cell Banks for peptide presentation

Most are autologous products with exceptions of MSC and MCBs

Third-party virus-specific T cells for the treatment of double-stranded DNA viral reactivation and posttransplant lymphoproliferative disease after solid organ transplant

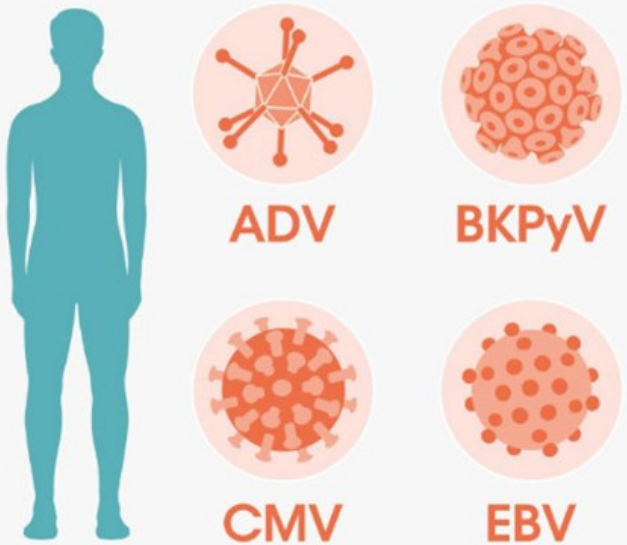
Are virus-specific T cells (VST) a safe and effective therapy for viral infections in SOT recipients?



Open label, phase II trial

98 SOT recipients

Quadrivalent third-party VST infusions for:



Median: 2 infusions per patient

Overall response rate:

- 68% ADV
- 45% BKPyV
- 65% CMV
- 61% EBV

Of patients with postTx lymphoproliferative disorder:

- 20% had a complete response
- 40% had a partial response

AJT

Recruiting

CD79b-19 CAR T Cells in Non-Hodgkin Lymphoma

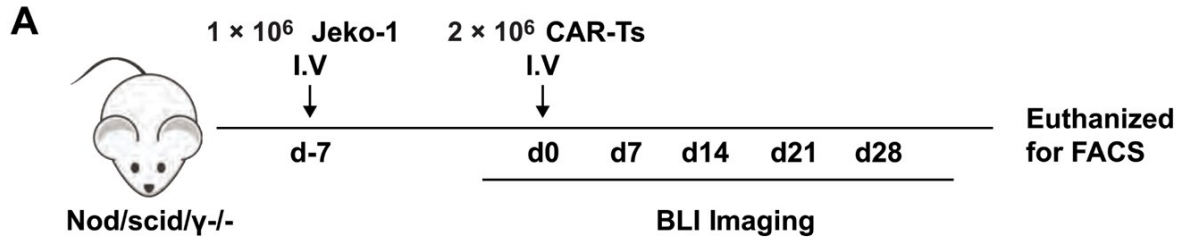
ClinicalTrials.gov ID NCT06026319

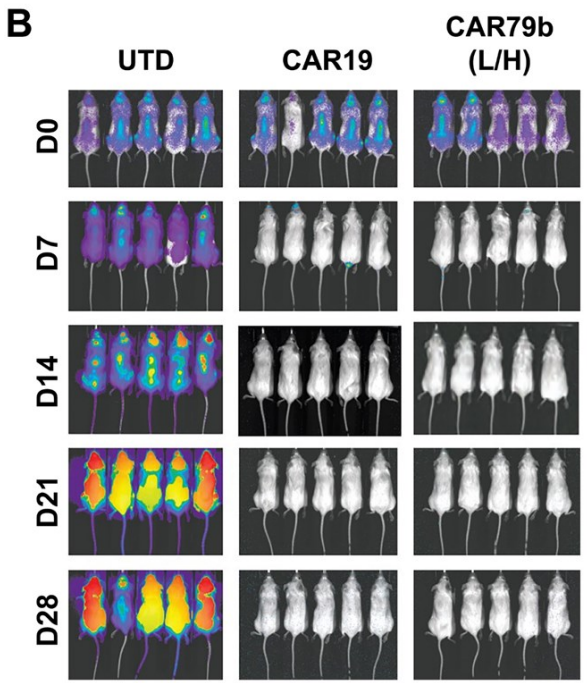
PRECISION MEDICINE AND IMAGING | DECEMBER 01 2019

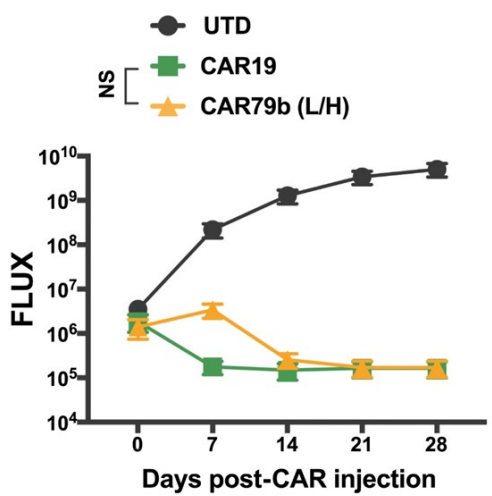
Chimeric Antigen Receptor T Cells Targeting CD79b Show Efficacy in Lymphoma with or without Cotargeting CD19 FREE

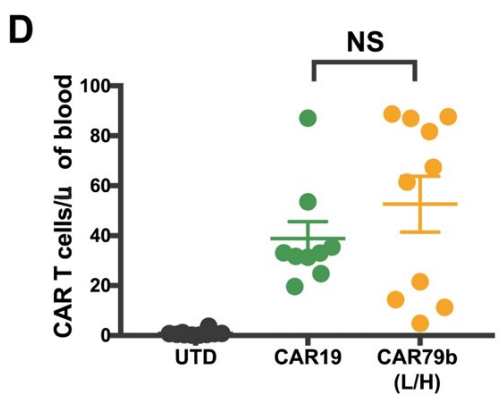
Marcella Maus, MD

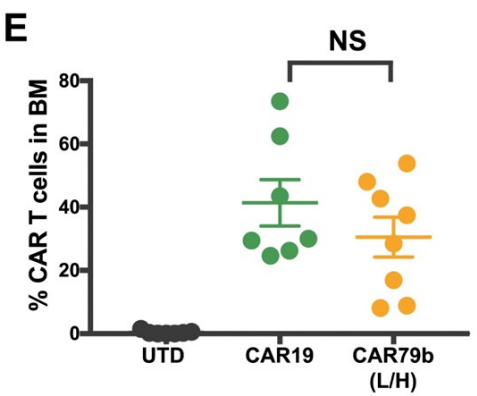
Dana-Farber Cancer Institute







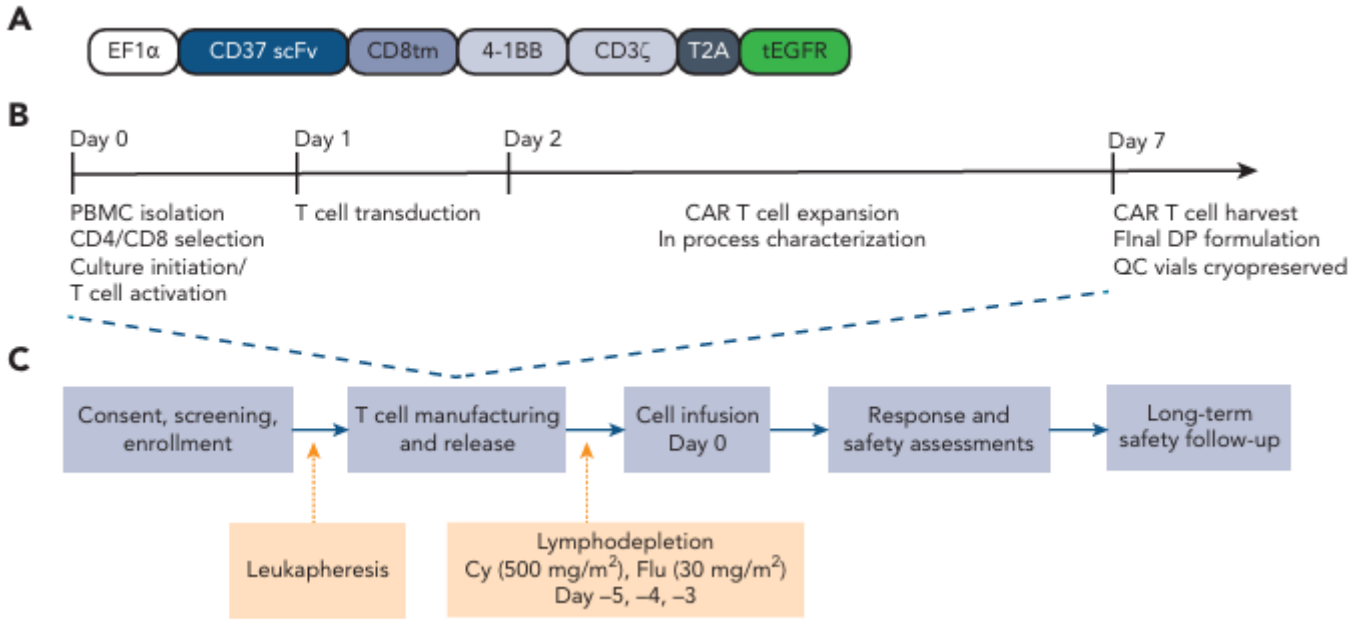




Completed

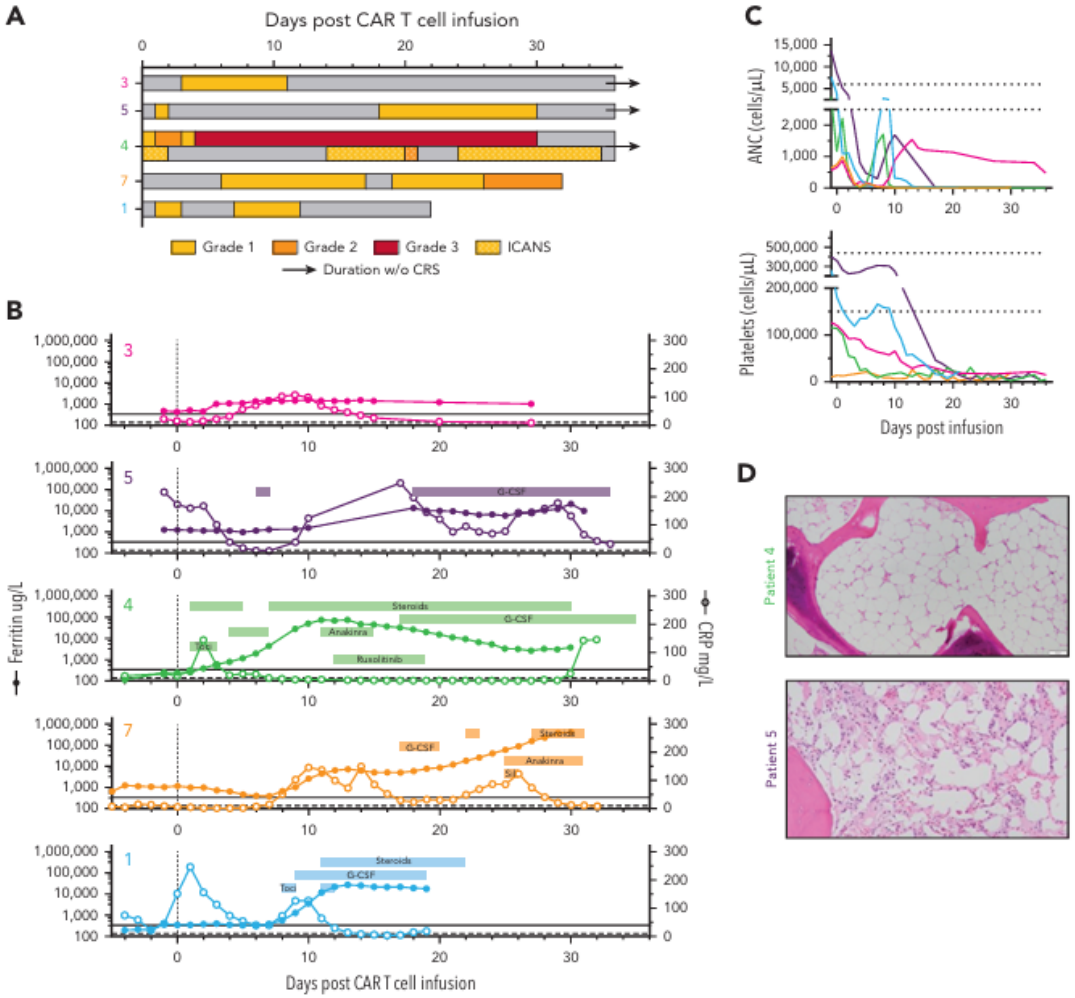
CAR-37 T Cells in Hematologic Malignancies

ClinicalTrials.gov ID NCT04136275



CLINICAL TRIALS AND OBSERVATIONS

Phase 1 study of CAR-37 T cells in patients with relapsed or refractory CD37+ lymphoid malignancies



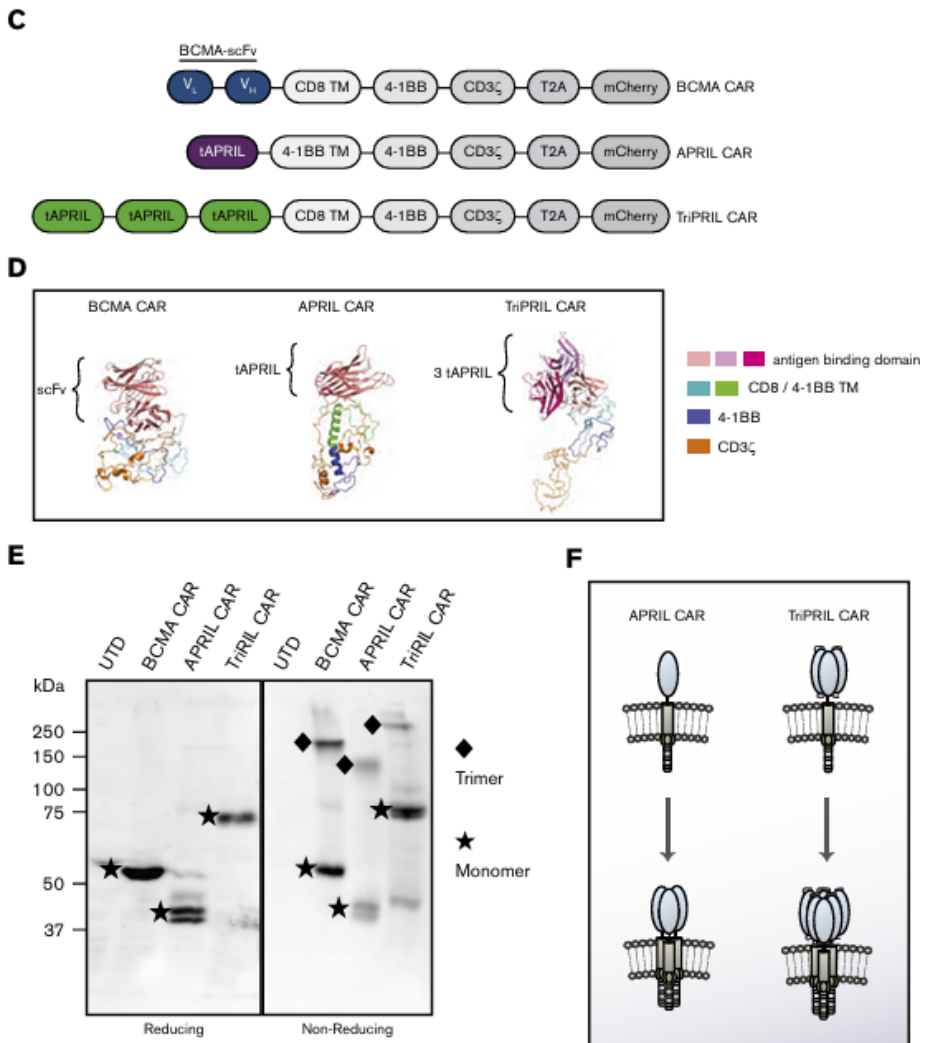
Marcella Maus, MD

Dana-Farber Cancer Institute

Recruiting

TriPRIL CAR T Cells in Multiple Myeloma

ClinicalTrials.gov ID NCT05020444



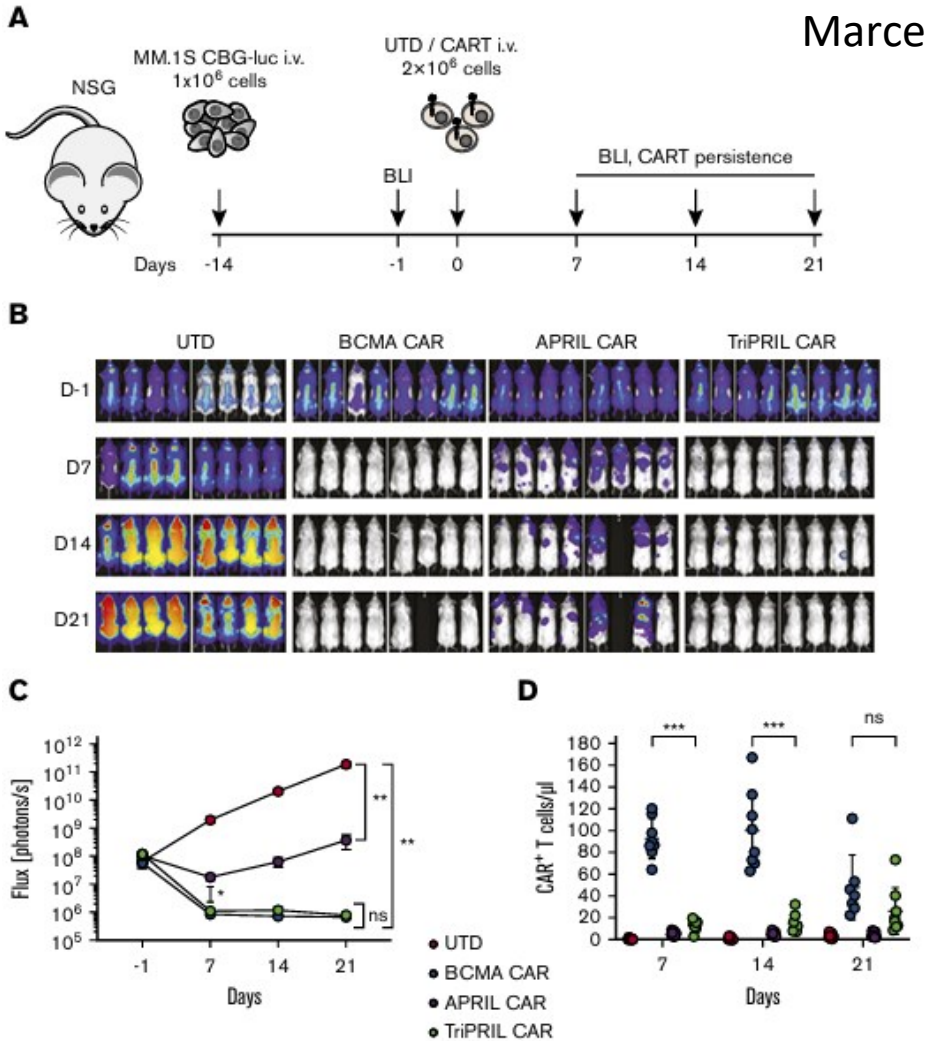
REGULAR ARTICLE

blood advances

Check for update

Rational design of a trimeric APRIL-based CAR-binding domain enables efficient targeting of multiple myeloma

Marcella Maus, MD



Recruiting

CARv3-TEAM-E T Cells in Glioblastoma

ClinicalTrials.gov ID NCT05660369

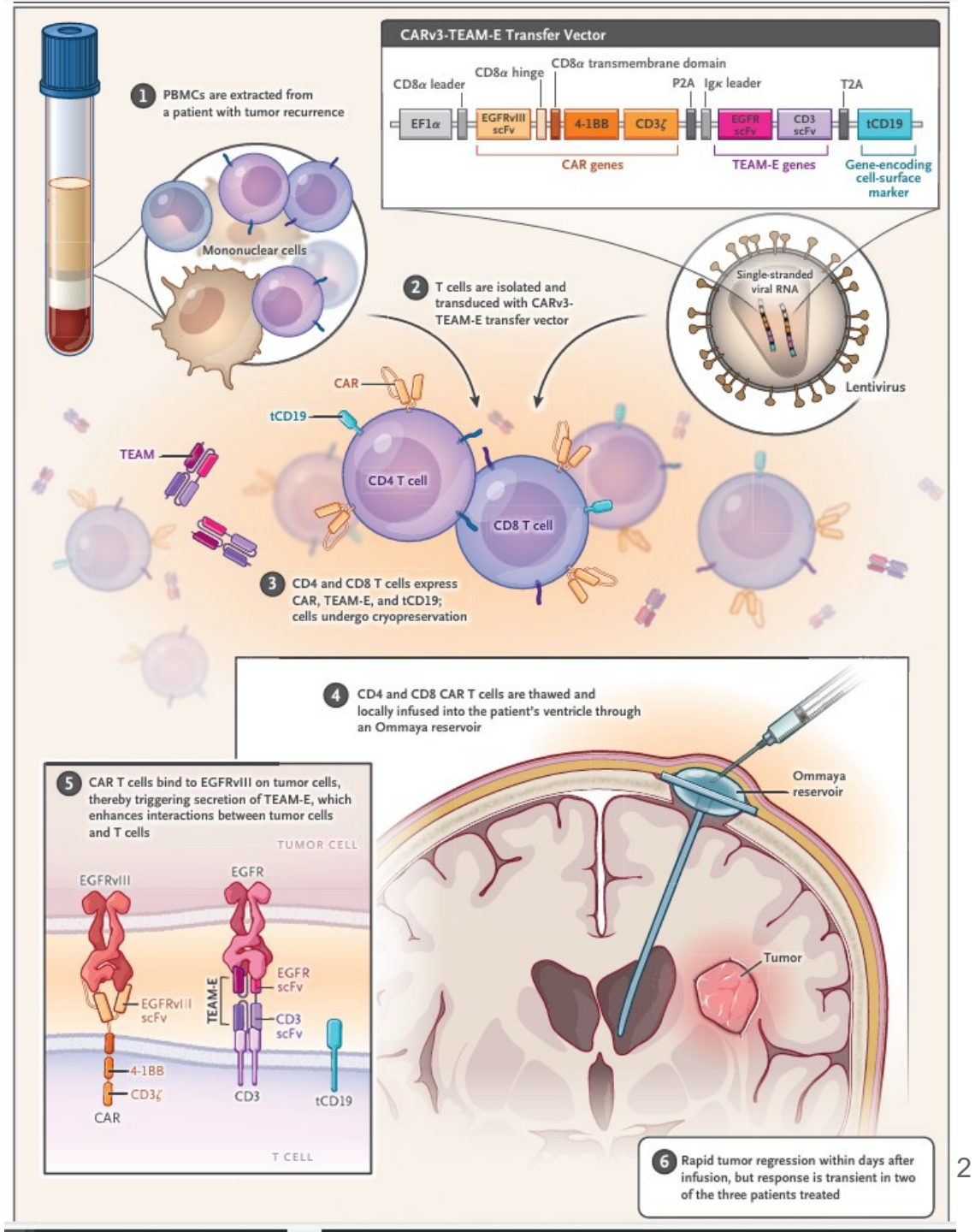
The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

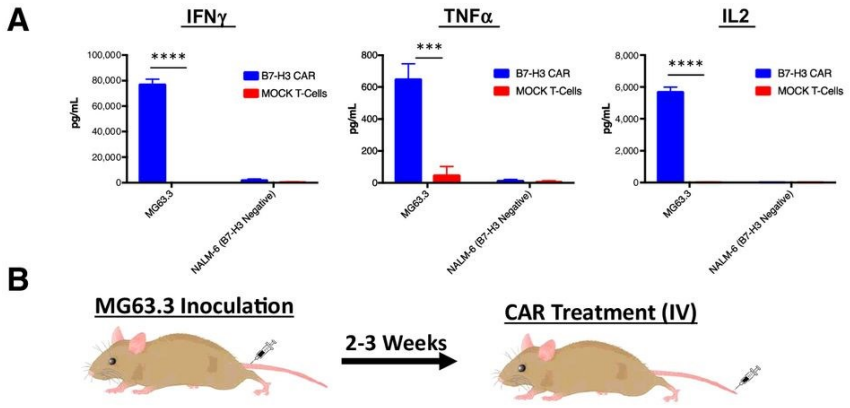
Intraventricular CARv3-TEAM-E T Cells in Recurrent Glioblastoma

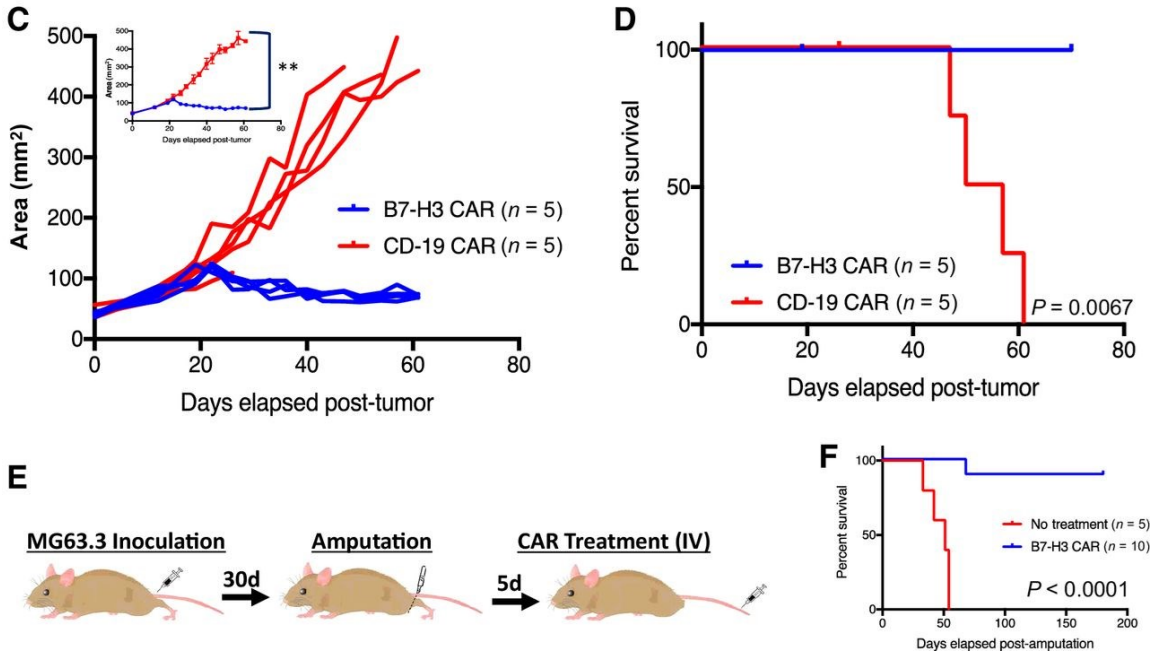
Marcella Maus, MD

Dana-Farber Cancer Institute



Tech transfer of a new B7-H3 CAR-T in glioma





TRANSLATIONAL CANCER MECHANISMS AND THERAPY | APRIL 15 2019

CAR T Cells Targeting B7-H3, a Pan-Cancer Antigen, Demonstrate Potent Preclinical Activity Against Pediatric Solid Tumors and Brain Tumors FREE

nature medicine

Article

https://doi.org/10.1038/s41591-024-03451-3

Intracerebroventricular B7-H3-targeting CAR T cells for diffuse intrinsic pontine glioma: a phase 1 trial

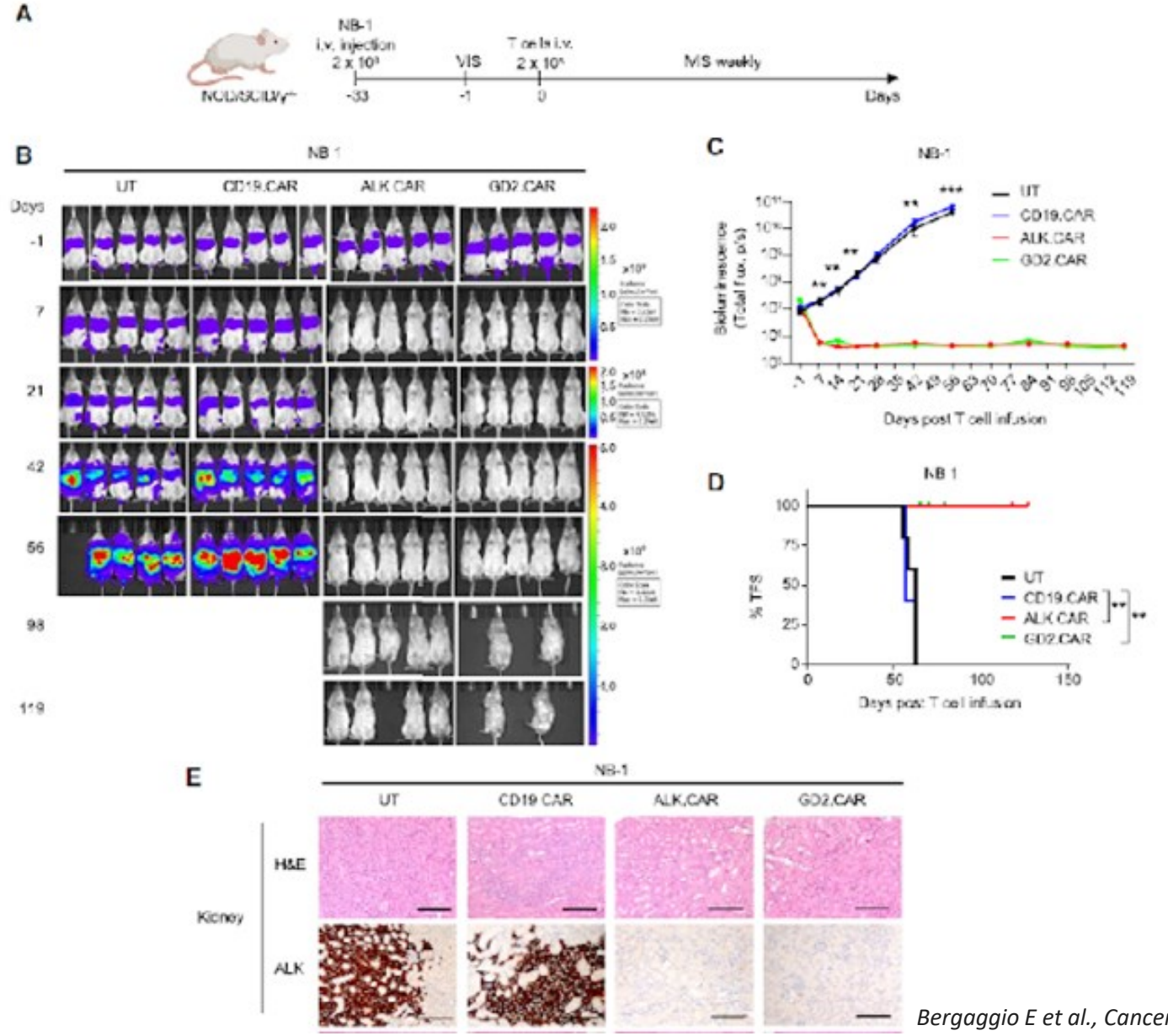
Robbie Majzner, MD

Dana-Farber Cancer Institute

From Pre-Clinical to Clinical:

Practical problems you may encounter

Case Study: Onboarding CAR T cells for Neuroblastoma

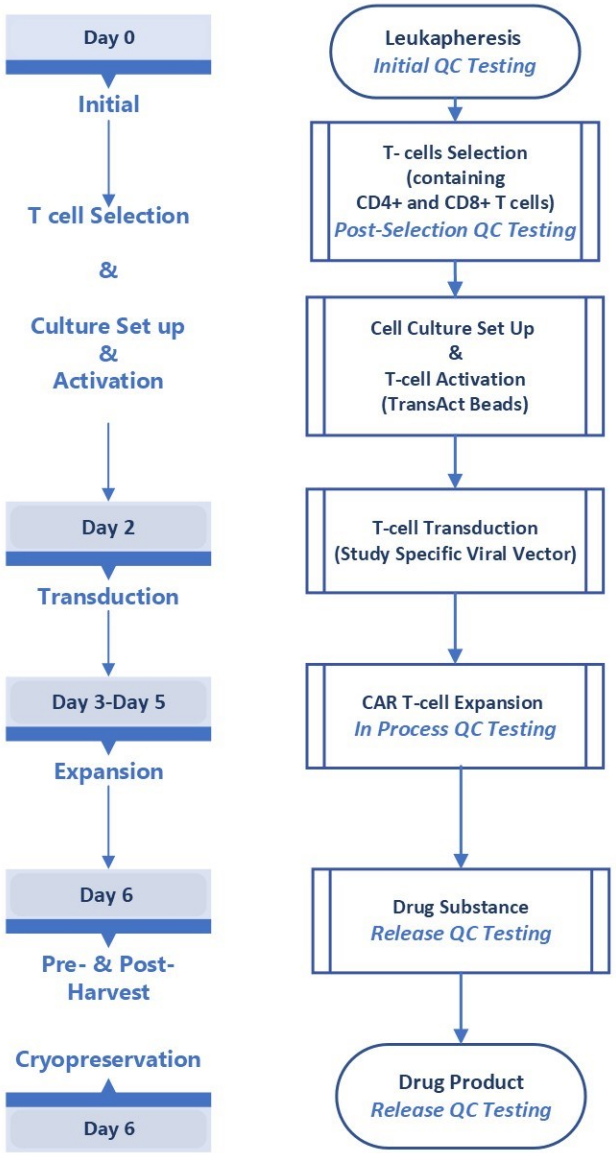


- Dr. Chiarle's lab generated ALK.CAR vector: target the ALK receptor selectively expressed by Neuroblastoma cells and showed that their efficacy depends on the abundance of ALK receptor on the surface of tumor cells
- Tested the anti-tumor activity in a mouse model of ALK driven Neuroblastoma
  - Ffluc transduced NB-1 in NSG
  - CAR = CD28 costimulatory endodomain
  - Transduction efficiency= 50%
- UT= Untreated Group
- CD19.CAR= Negative Control
- ALK.CAR= Test Group
- GD2.CAR= Positive Control

Bergaggio E et al., Cancer Cell. 2023. doi: 10.1016/j.ccell.2023.11.004. Epub 2023 Nov 30.

Case Study: Onboarding the New CAR T Study

✔ Manufacturing Process:



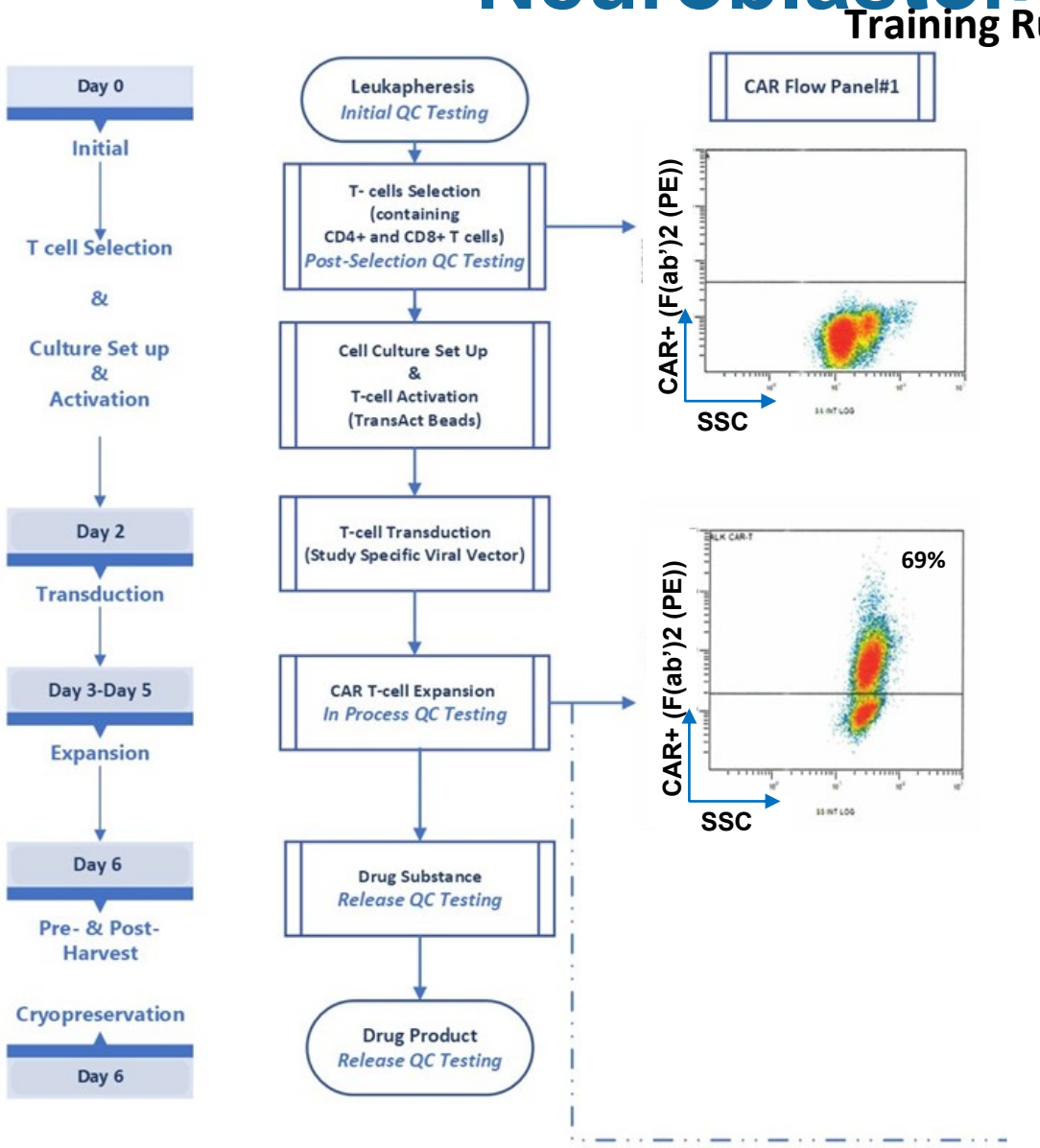
Assay Validations:

Common Assays used for CAR T

Tests	Platform Validated
Cell Count	✔
Viability	✔
Transduction Efficiency	✔
RCR/RCL	✔
Flow cytometry	✔
VCN assay	✔
Mycoplasma	✔
Endotoxin	✔
Sterility (BacT ALERT)	✔
Potency	-
Other	-

Dana-Farber

Case Study: CAR T cells Manufacturing for Neuroblastoma in CMCF

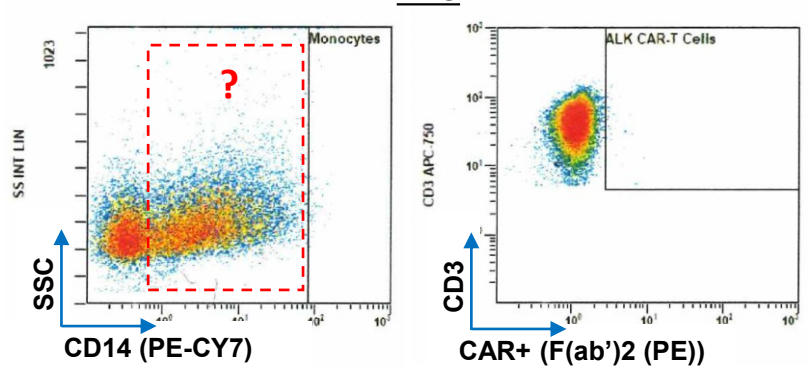


Training Run #1

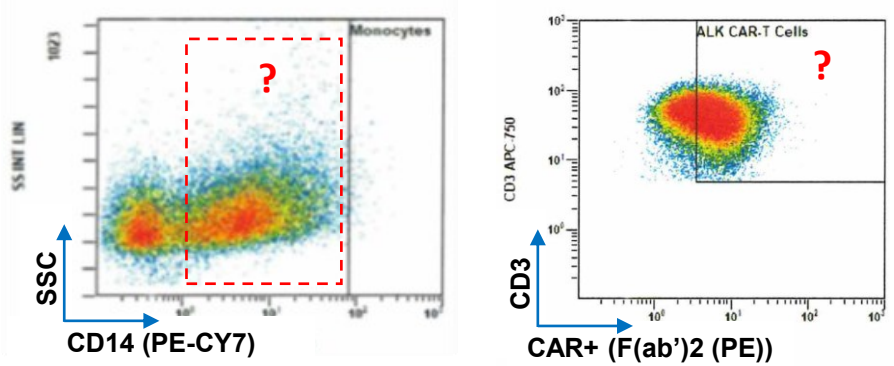
Case Study: Troubleshooting CAR Flow Panel #2

Step 1: define issue

FMO



Sample



Step 2:

- connected with CAR+ AB manufacturer
- shared available data
- and followed suggestion:
  - Fc blocking
  - order a new AB with different fluorochrome as PE fluorescence protein could stick to the cells
  - add goat/human/rabbit serum to the staining buffer

Step 3:

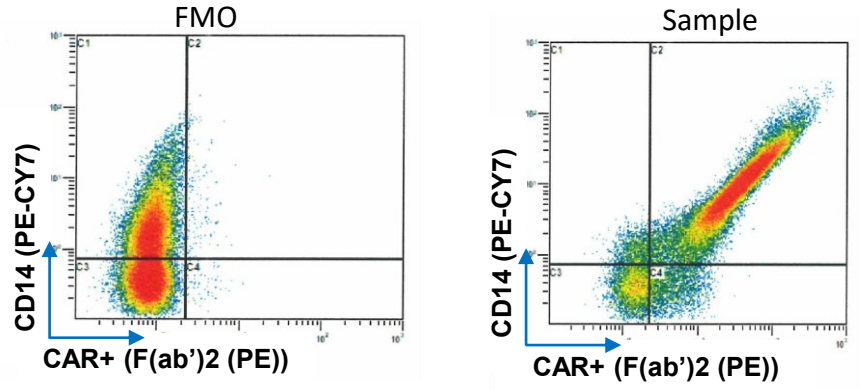
- informed Sponsor and shared current troubleshooting plan
- brainstorm back up plan(s)

Considering:

- Timeline?
- Acceptable to FDA?
- Cost effective?

Case Study: Addressing Non-Specific/ Unwanted AB Binding

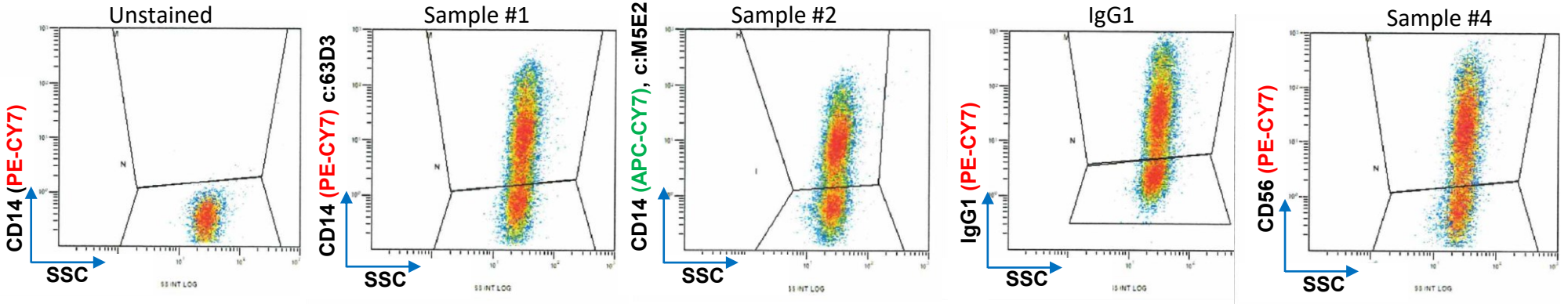
Troubleshooting #1



CAR+ cells = CD14 PE-Cy7?

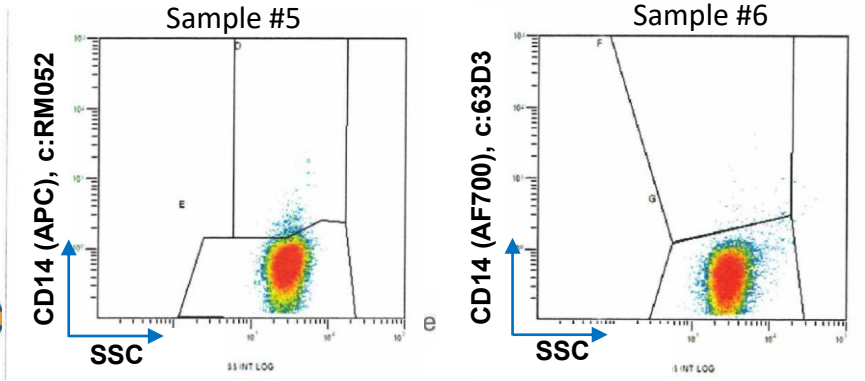
Fluorochrome	CD-	Clone	Pos / Neg
PE-Cy7	CD14	63D3	+
APC	CD14	RMO52	-
APC-Cy7	CD14	M5E2	+
AlexaFluor700	CD14	63D3	-
PE-Cy7	CD56		+
PE-Cy7	IgG1		+

Troubleshooting #2



CAR+ cells =-Cy7?

Troubleshooting #3

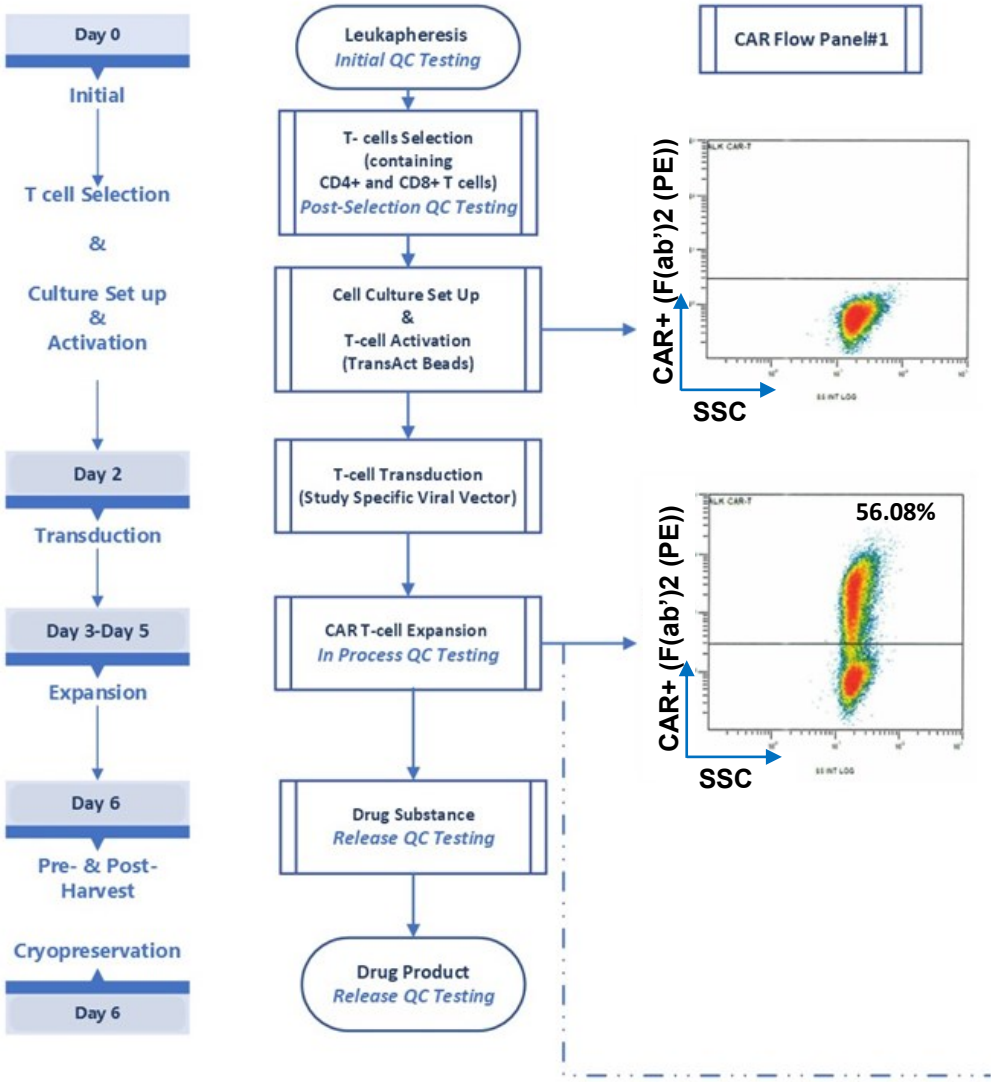


CAR+ cells bind to -Cy7

Progress:
Company Field Specialist:
"I think we need to start from scratch"
Sponsor: *"Timeline?"*
CMCF *:*
"Let's replace AB containing –Cy7 and try again"

Case Study: Replace CD14 PE-Cy7 with CD14 APC

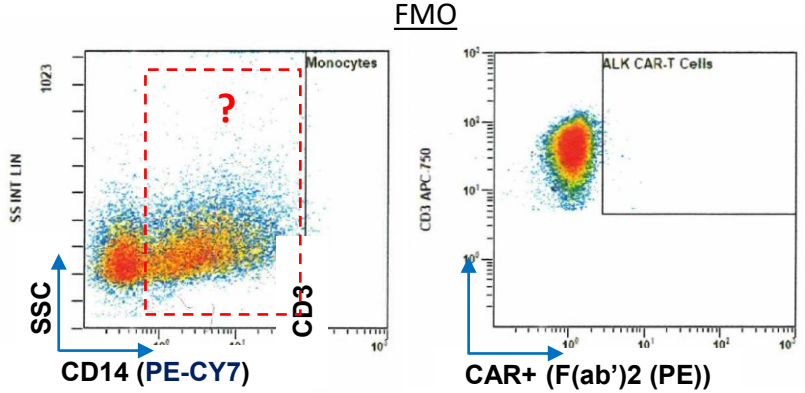
Training Run #2



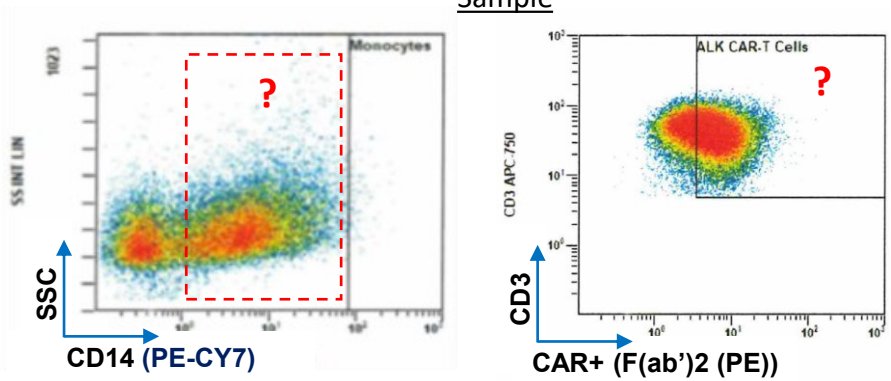
Case Study: CAR Flow Panel #2 Final Touch

Conclusion1 :
non-specific/
undesired
binding

FMO



Sample



FMO

Sample

Recruiting

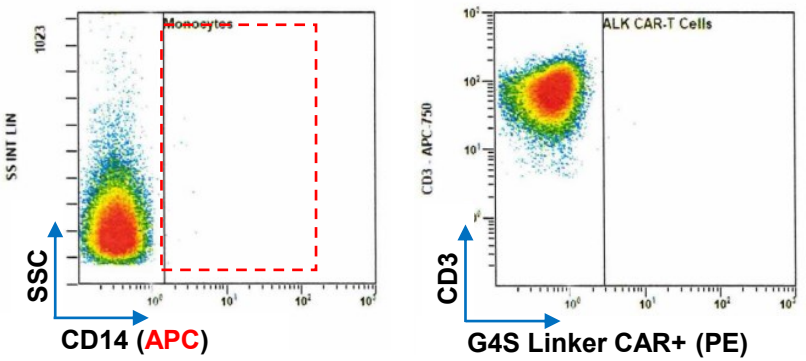
CAR

Study of hALK.CAR T Cells for Patients with Relapsed/refractory High-risk Neuroblastoma

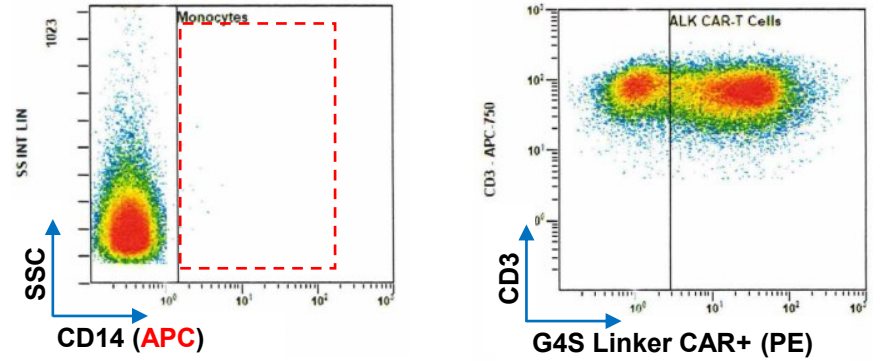
ClinicalTrials.gov ID NCT06803875

Conclusion 3:
✔ Safety & Use
G4S linker

FMO

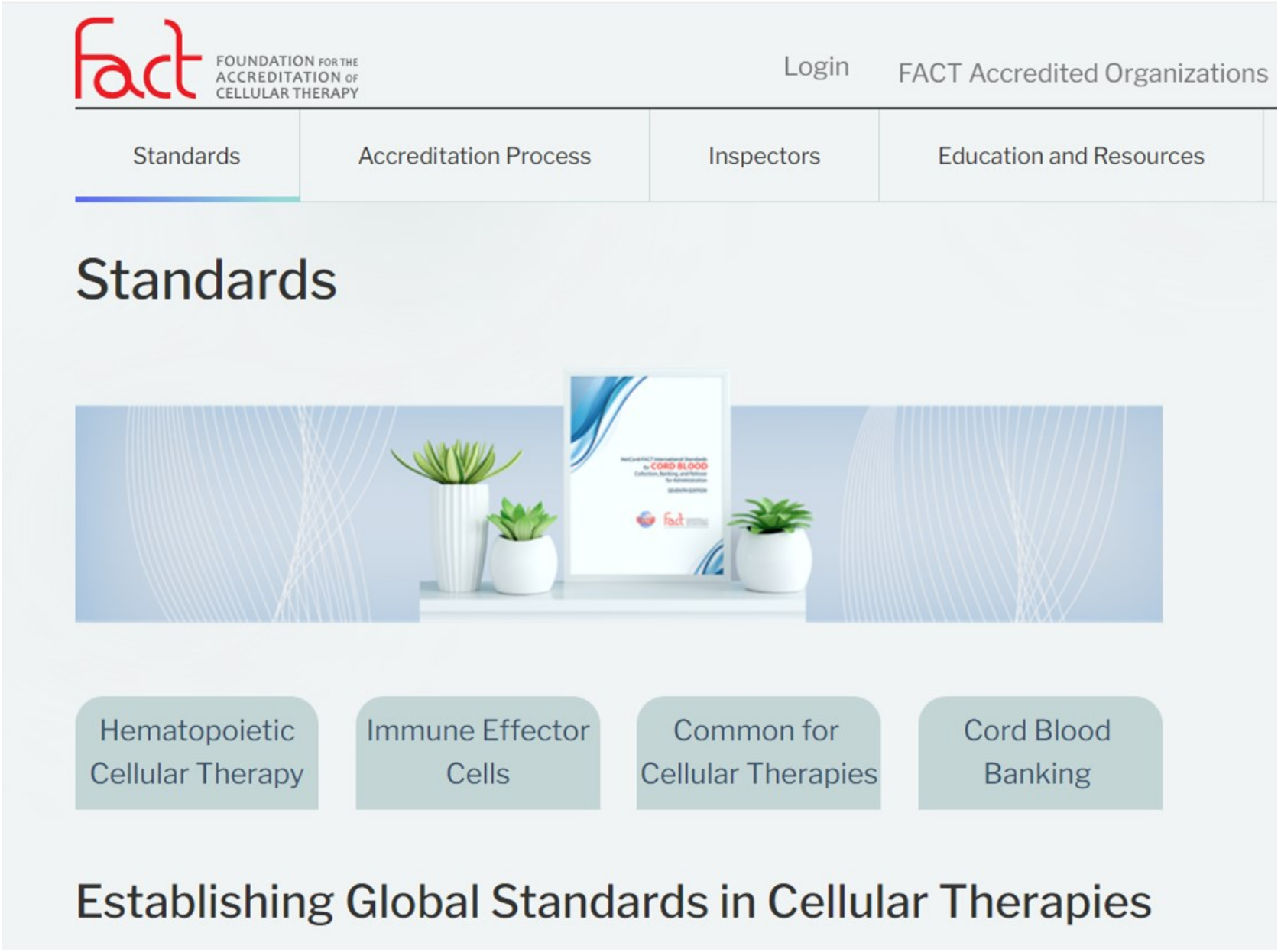


Sample



Dana-Farber Cancer Ins

Certification and Accreditation of professionals and clinical and manufacturing sites



- **Foundation for the Accreditation of Cellular Therapy**

- Accreditation body for multiple types of cell therapy for decades

- Designed to ensure quality standards but vetting internal quality management systems – including education, availability of qualified staff and resources, and continual data review

- All aspects of chain – apheresis, cell processing lab, clinical program

Growing AABB's Biotherapies Footprint

Credentialing the Workforce

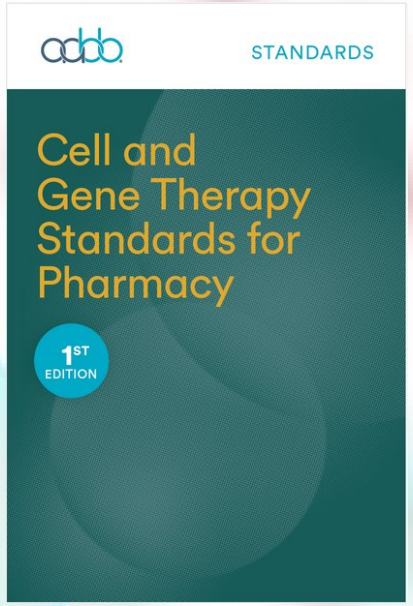
The Certified Advanced Biotherapies Professional (CABP) program continues to grow.
150 credentialed, with over 50 more in progress.

CABP

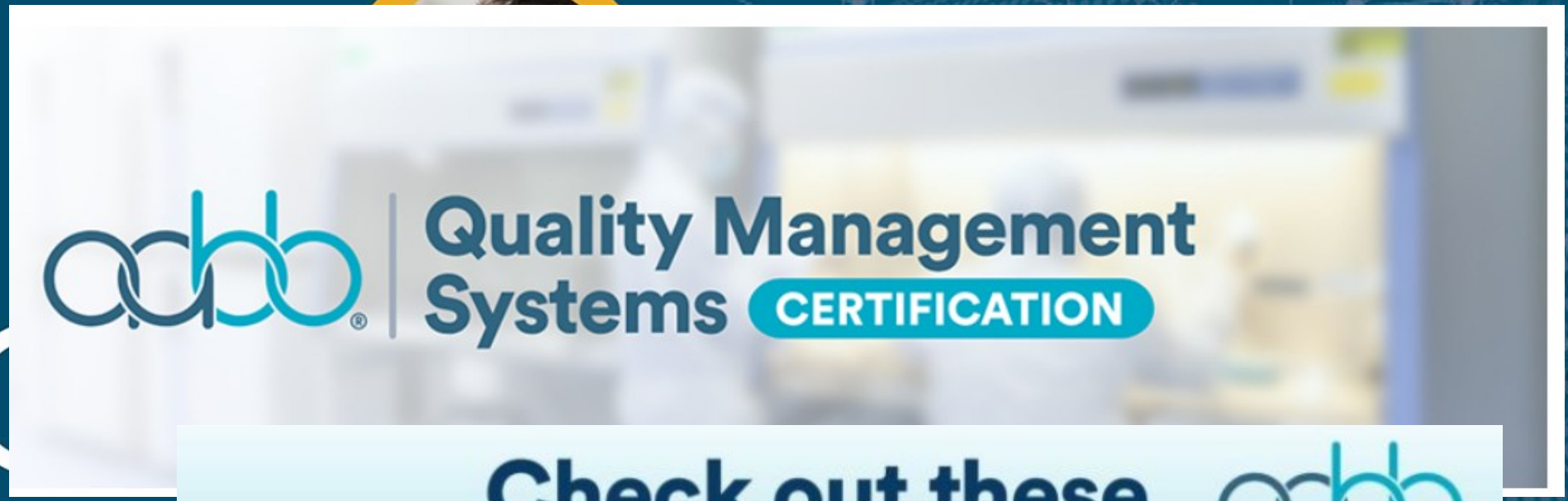
AABB | Certified Advanced Biotherapies Professional

Raising the Bar in Accreditation and Standards

12th ed. of Cellular Therapy Standards **effective July 1, 2025, expanding focus on critical technology considerations, returned and reissued products.**



New Accreditation Program: *Cell & Gene Therapy Standards for Pharmacy*



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AABB's M
Improving liv
biotherapies

AABB's V
A connected
transfusion m
patient. From

Check out these AABB Publications

AABB Biotherapies Manual Coming Soon!

Cell & Gene Therapy: 2026

1. Ten years ago, groundbreaking, lifesaving and ‘transformative CGTs started being developed.
2. Today, the industry has realized much of that potential. CGTs have evolved from proof-of-concept to commercialized treatments, from pre-clinical concepts to reality.
3. In 2025, 43 FDA approvals and expansion of indications of earlier treatment lines.
4. The Industry is buzzing with new breakthroughs and technical/biological developments.
5. However, several concerns in the horizon seem to be harder-than-expected to fix.

The biggest challenges in cell and gene therapy: Global Accessibility

1. Making CGTs affordable and commercially viable
2. Each country is different, with different needs, regulatory framework and different expectations on outcome
3. Improving patient-specific supply chains
4. Standardization of Material Collection and Product Administration, at clinical sites and manufacturing processes
5. Standardization of QC and potency assays and processes.
6. Better, faster, cheaper!

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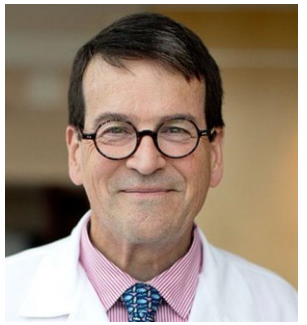

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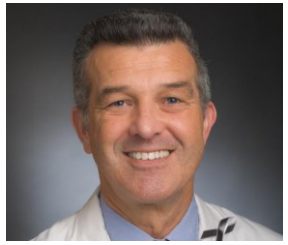

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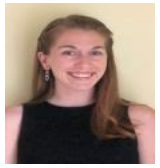

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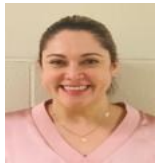

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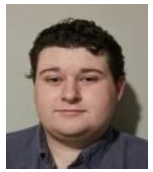

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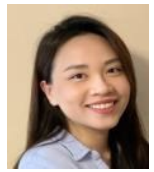

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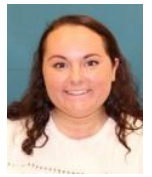

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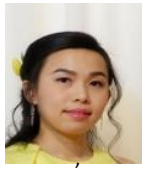

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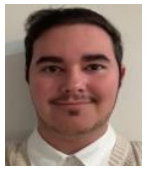

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Preguntas & Respuestas