

Disclosure

Collaborative Research Agreement with
Celgene for Developing CAR Studies
Managed by Baylor College of Medicine



Center for *Cell and Gene Therapy*

Genetically Engineered T cells for
Cancer Immunotherapy

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Assistant Professor, Pediatrics



CAGT - Component Parts

Clinical Study
Resources



Clinical Treatment &
Research

GMP
&
VPF



Basic & Translational
Research

Resources for Clinical Studies

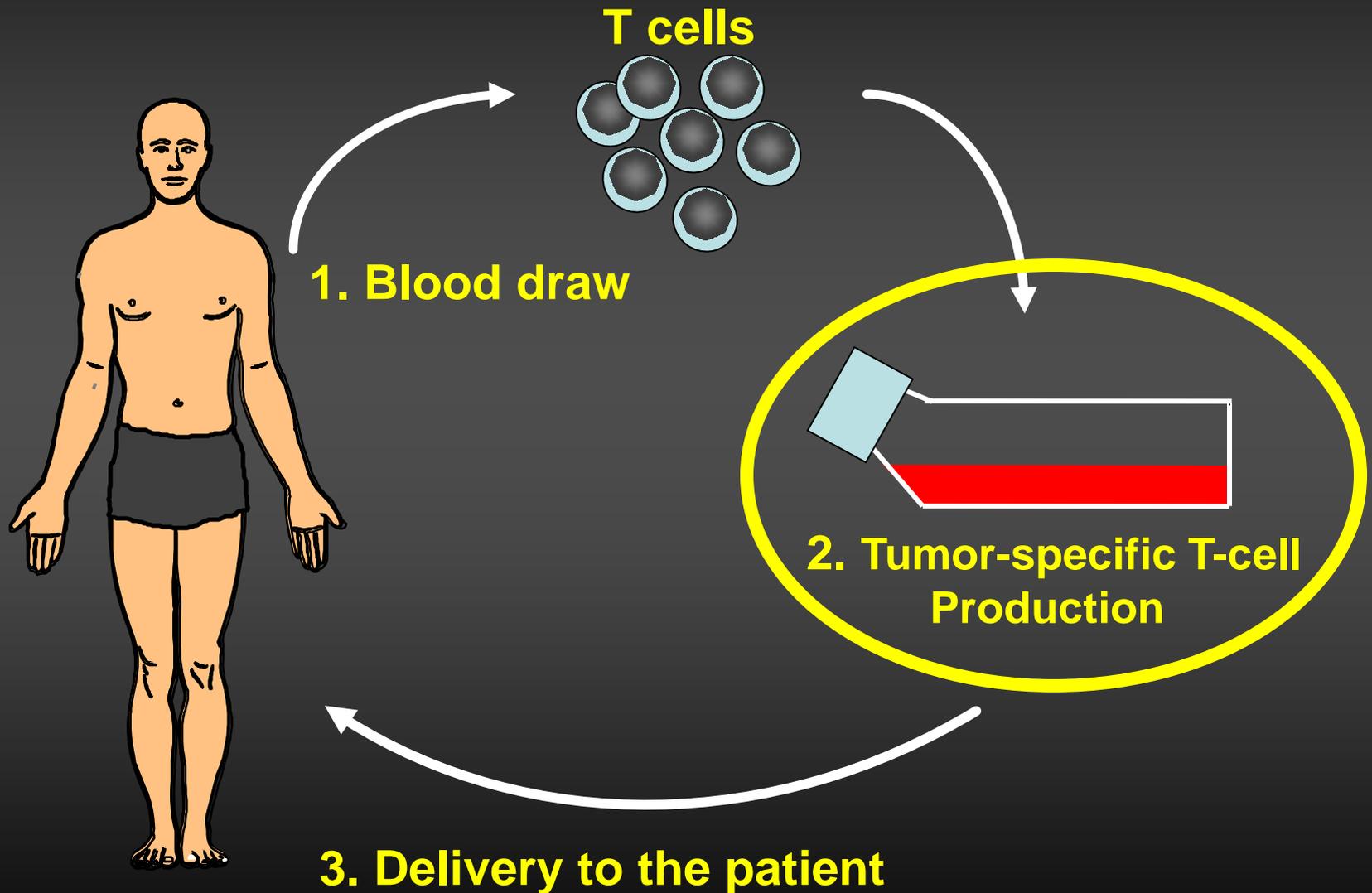
- **Regulatory affairs staff**
 - Submissions
 - SAEs and annual reports
- **Research co-ordinators**
 - Study logistics, data management
- **Quality control**
 - On going study monitoring
- **Quality assurance**
 - Study audits



Trial Description

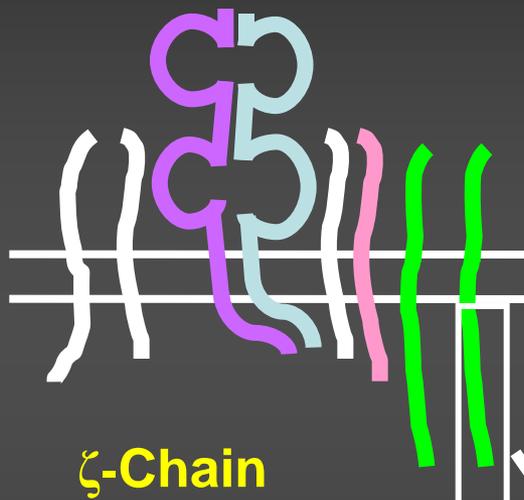
- Investigator-initiated
- Phase 1 >>> Phase 2 at highest DL
- Gene transfer: redirect & modify T cells
- Retro-, Adeno- and Lentiviral vectors
- Accrual: Equal Access to Research
- Consenting: discuss study at time of procurement cells and preinfusion

Adoptive T cell Transfer

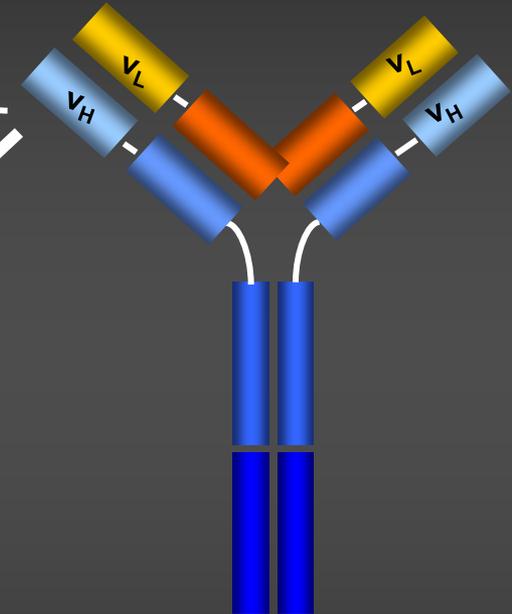


Chimeric Antigen Receptors

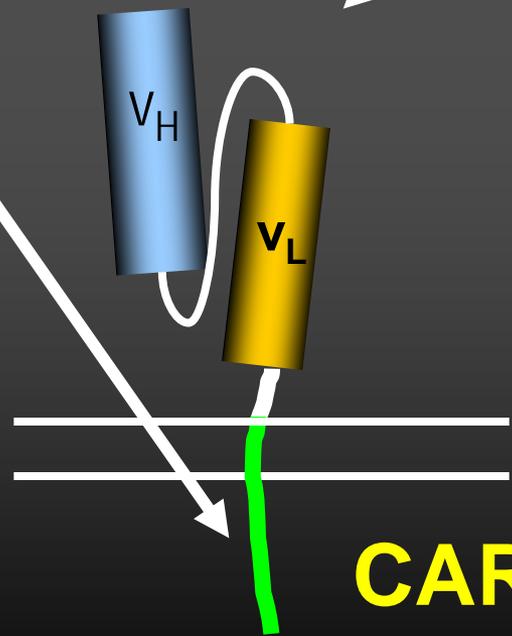
T cell Receptor



Variable Domain



Antibody

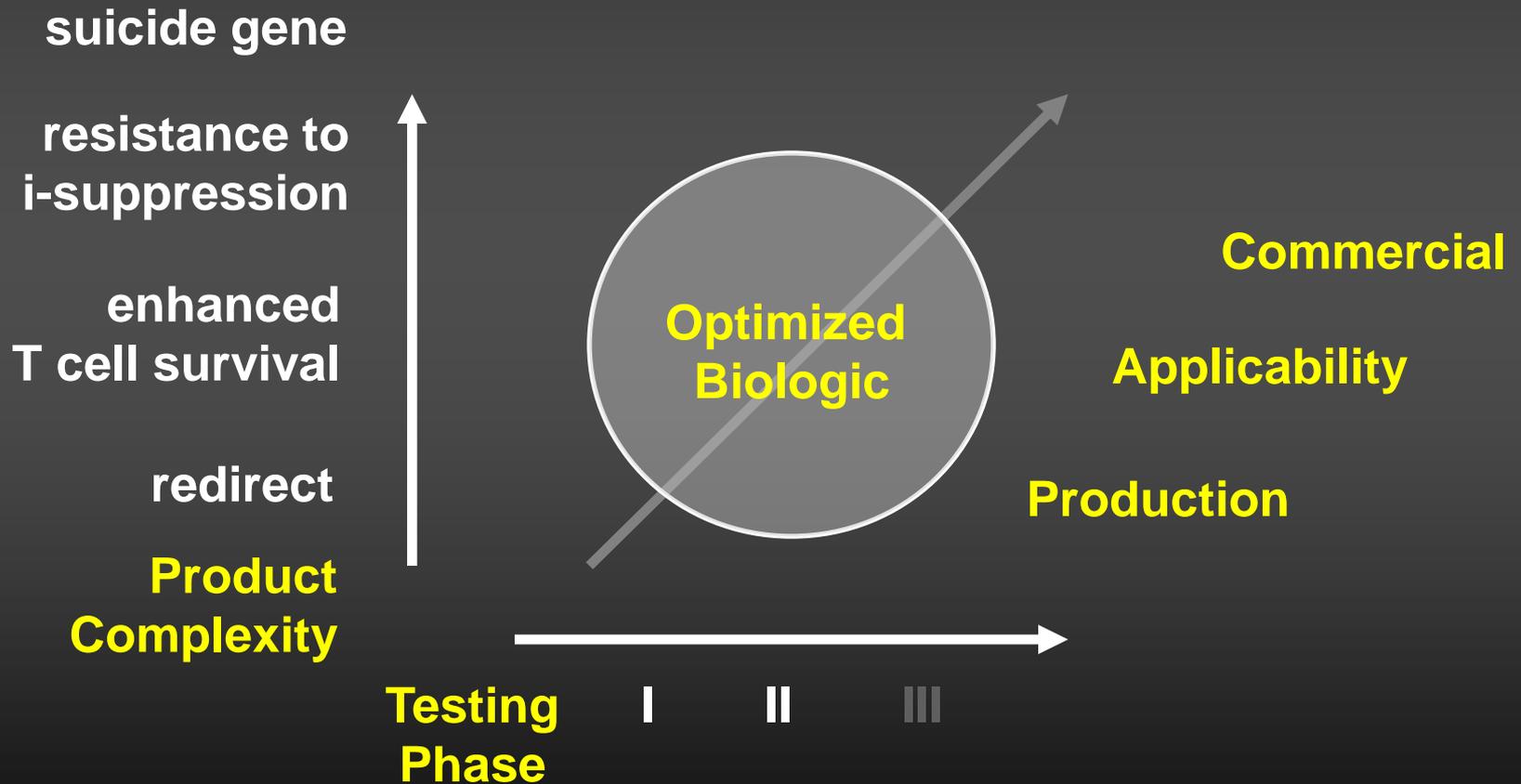


CAR

Studies with CARs

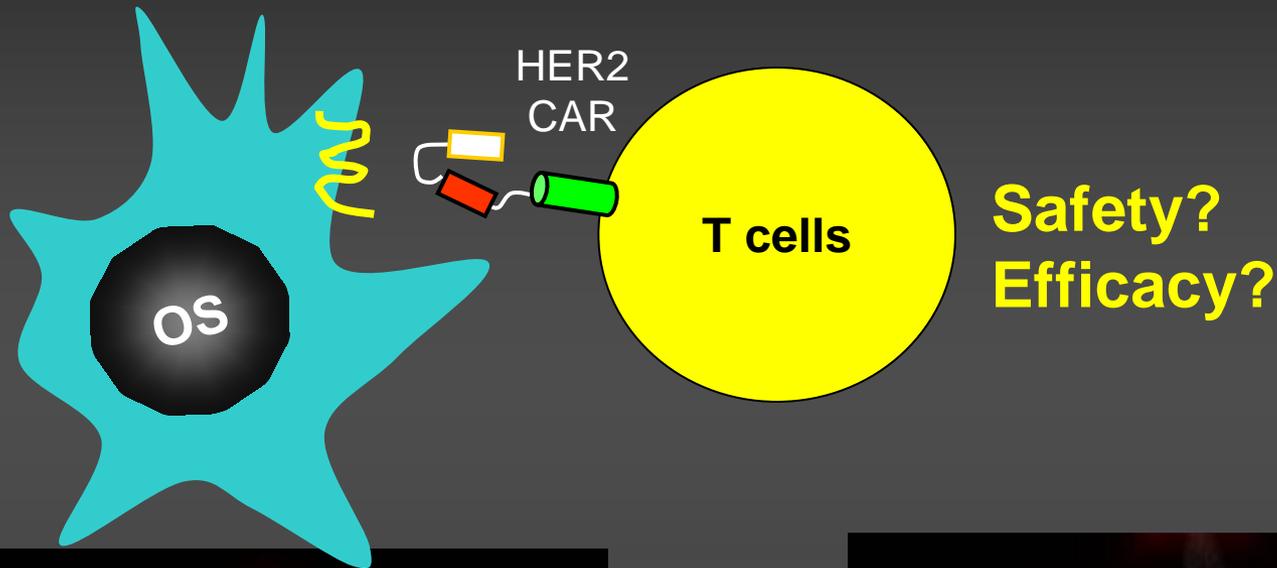
Target	Cancer	Investigators
CD19	Lymphoma, CLL, ALL	Gianpietro Dotti, Carlos Ramos
Kappa	Lymphoma, Myeloma	Gianpietro Dotti, Carlos Ramos
CD30	Hodgkin Lymphoma, ALCL	Barbara Savoldo, Helen Heslop
GD2	Neuroblastoma, sarcoma	Malcolm Brenner, Clio Rooney, Doug Myers (Kansas)
Her2 Neu	GBM, OS, Lung cancer	Stephen Gottschalk, Nabil Ahmed Malcolm Brenner
PSCA	Prostate cancer	Juan Vera, Ann Leen
MUC1	Breast cancer	Juan Vera, Ann Leen

Evolution of Engineered T cell Products



HEROS: NCT00902044

HER2 CAR T cells for OSteosarcoma



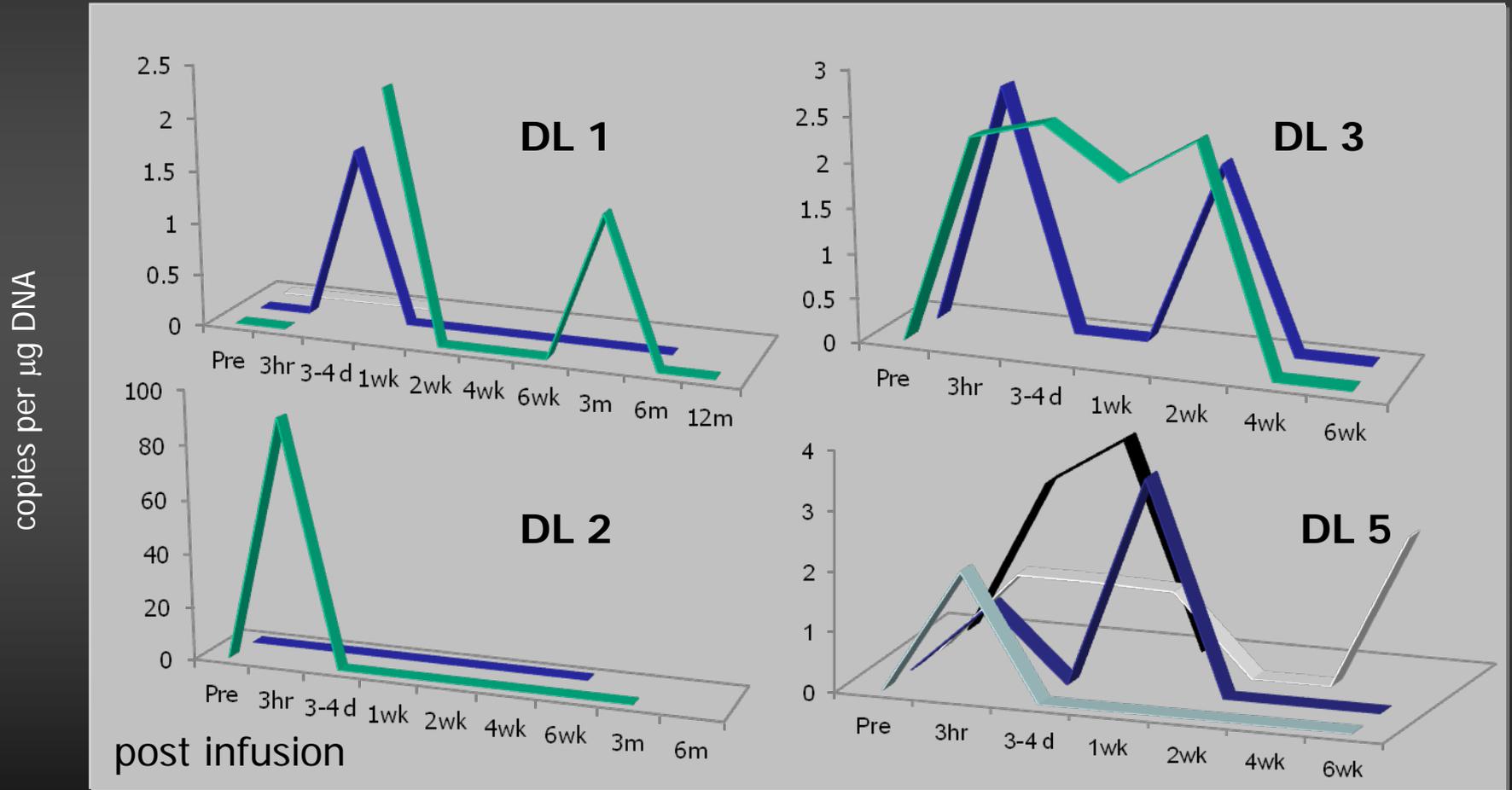
PREINFUSION

DL6
→



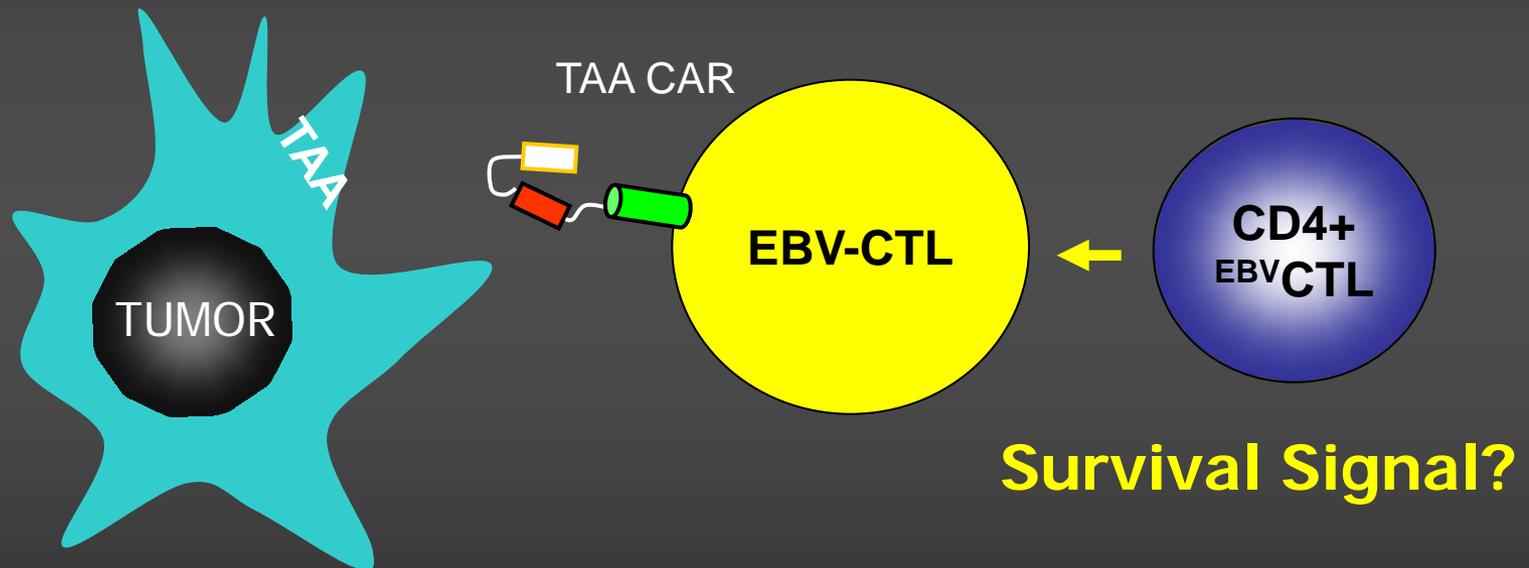
POSTINFUSION

HEROS: modest T cell persistence!



Enhancing T cell Survival

Grafting CARs on a Virus-specificity Platform



NESTLES

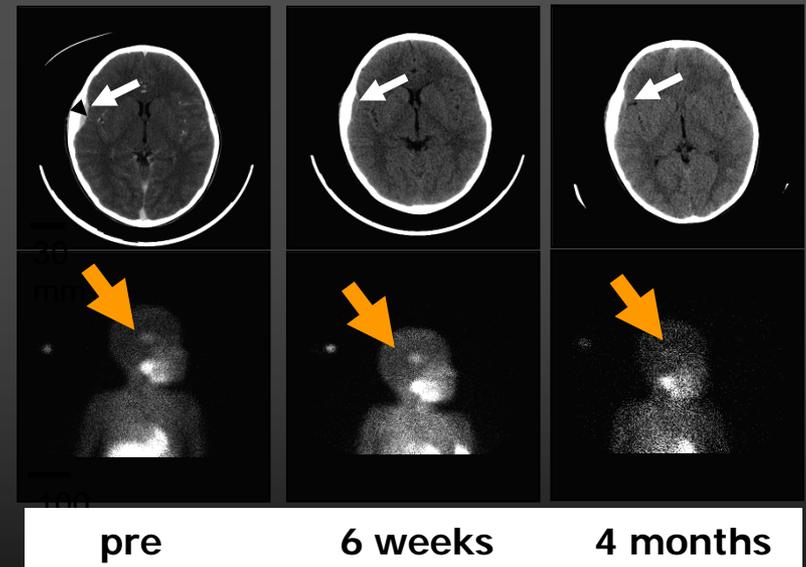
Peripheral blood T-cells and EBV-CTLs expressing GD2 specific CARs to subjects with Neuroblastoma

FDA IND 11217

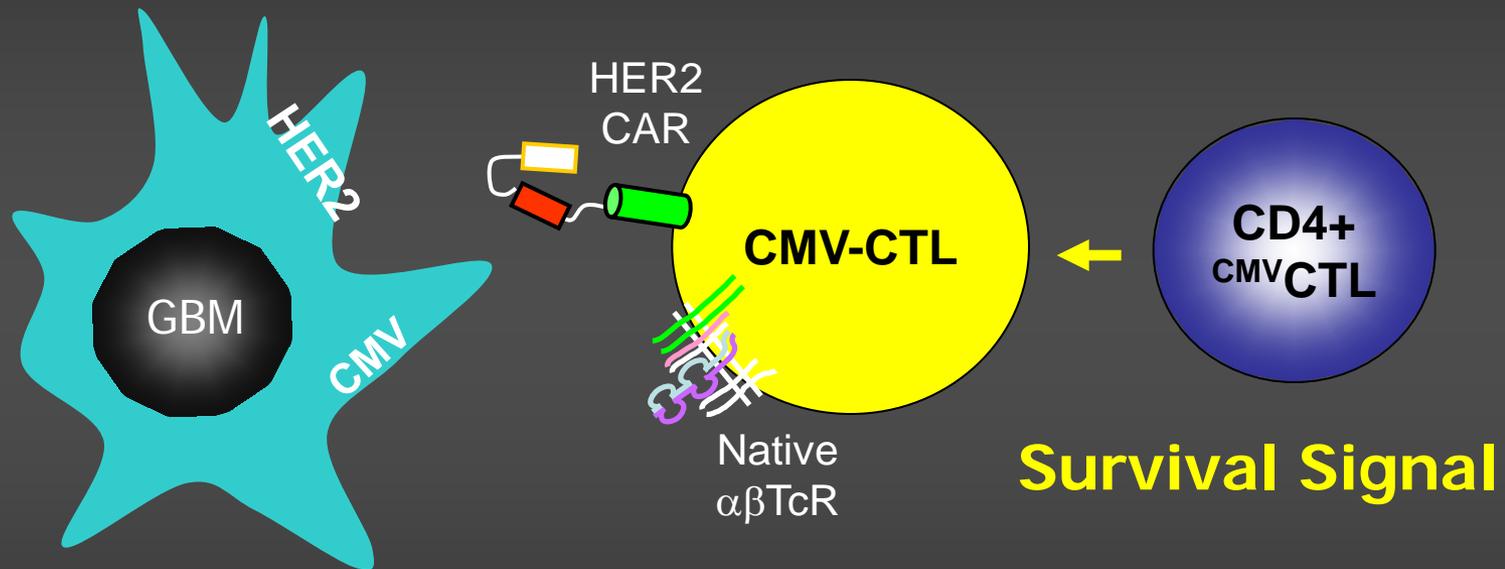
RAC 0212-563

Better short-term persistence of CTLs than activated T cells (ATC)

5/10 with evaluable tumors had tumor necrosis or regression; **2CR**



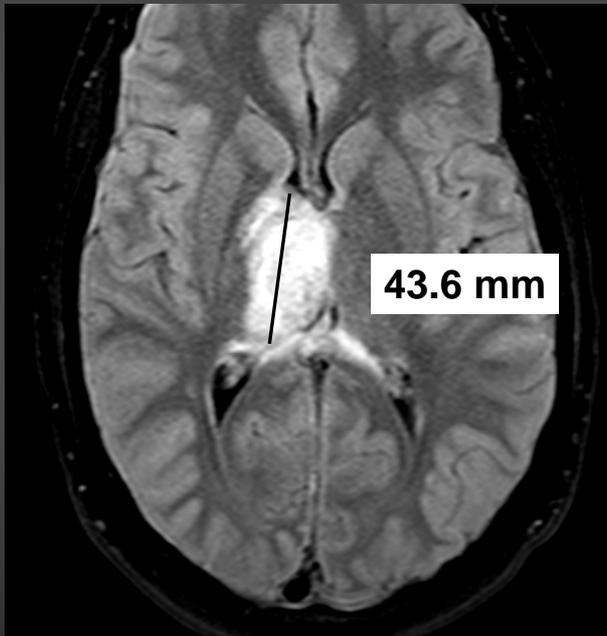
Targeting Multiple Antigens + Enhancing T cell Persistence



**Offset Tumor Escape
Activation Signal**

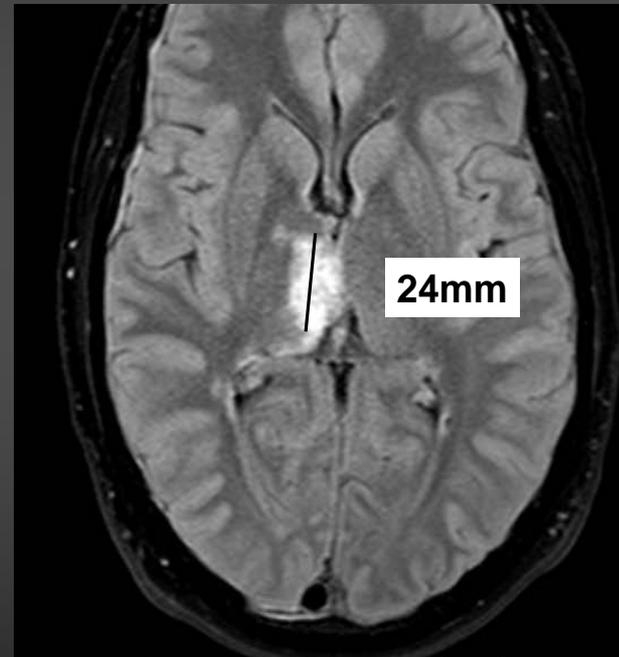
HERT-GBM: NCT01109095

HER2 CMV bispecific CTLs for Glioblastoma



PREINFUSION

DL1



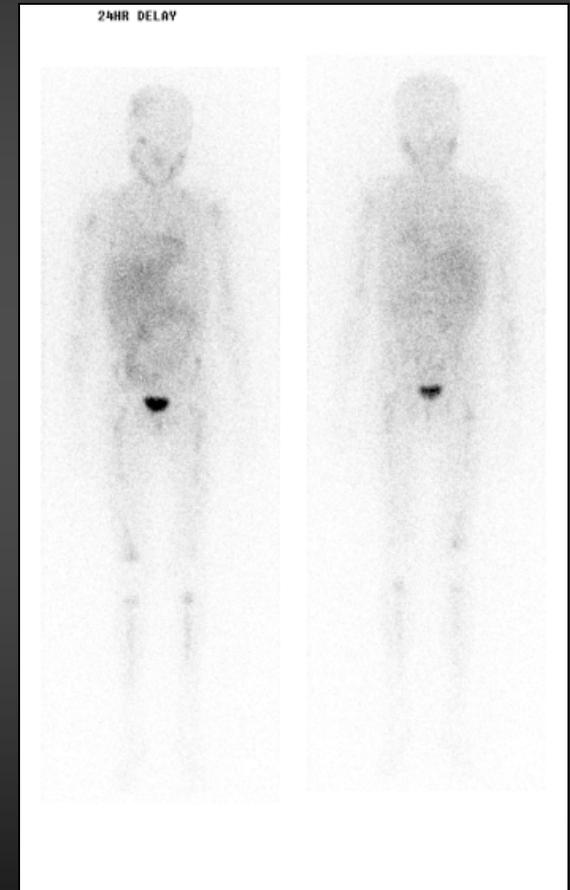
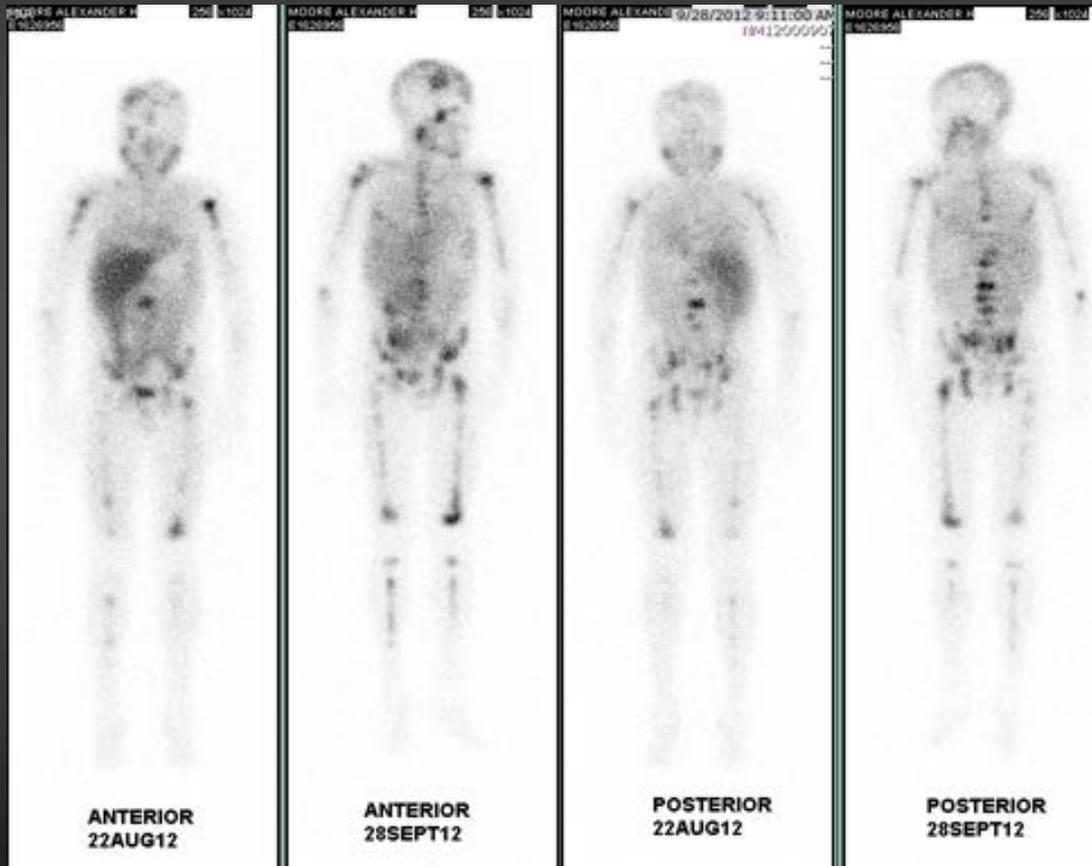
POSTINFUSION

Allo-HSCT and GD2.CAR Multivirus-CTL

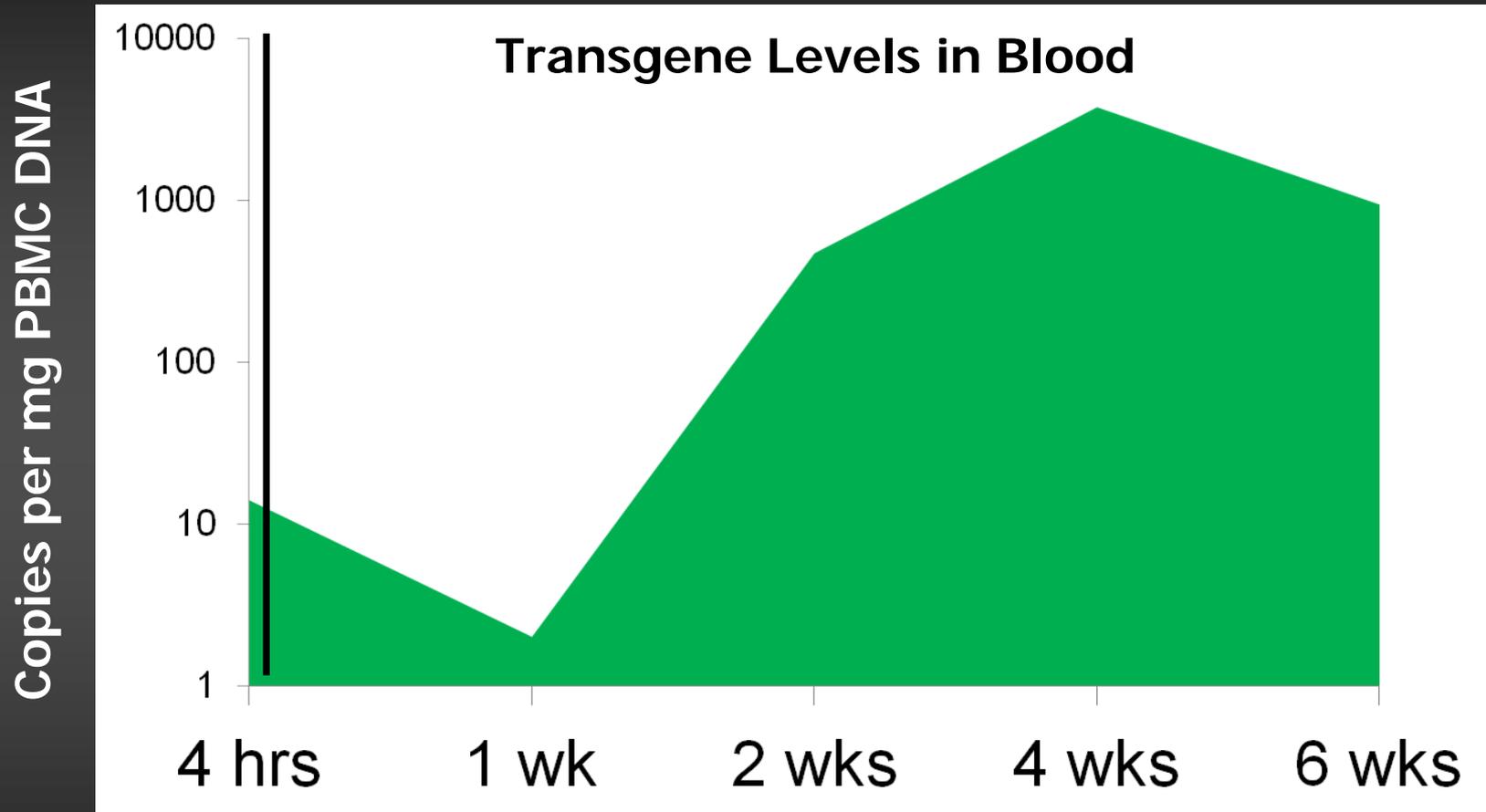
Pre-treatment

Post-transplant

9 wk Post-T cell



Allo-HSCT and GD2.CAR Multivirus-CTL



Post GD2.CAR-EBV-CTL infusion

Scientific Direction

1. T cell SURVIVAL & EXPANSION:

- Prephase

2. RAPID PRODUCTION:

- Peptide-based production

3. OFF-THE-SHELF PRODUCT:

- Closely-matched products

4. BROAD SPECTRUM products

- Targeting x-TAA & μenvironment

A Blood Bank Model: Multicenter Trial Closely Matched CTLs for Refractory Viral infection

CAGT: AM Leen, CM Bollard, A. Gee, MK Brenner, CM Rooney, HE Heslop

Other Sites

MDACC

EJ Shpall

Harvard

Joe Antin, B Dey

Duke

Paul Szabolcs

CHLA

Neena Kapoor

Children's Boston

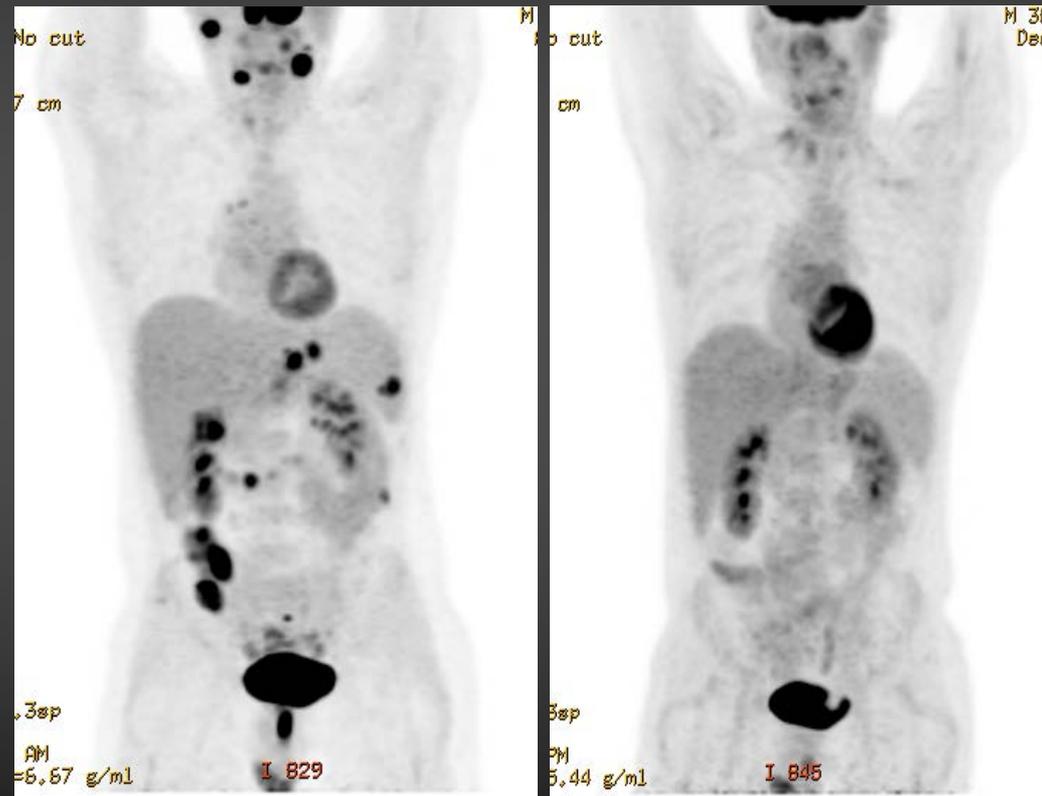
Sun Yun Pai

Miami

Gary Kleiner

Hackensack

Scott Rowley



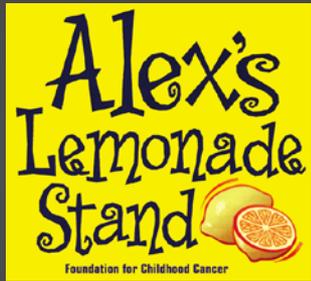
Commercialization

- **Bellicum** –successful Series B funding to commercialize caspase 9 suicide gene strategy
- **Cell Medica** received \$15M CPRIT grant and Series A financing for late phase studies of LMP1 specific T cells in lymphoma
- **Celgene** collaborative agreement with developing CAR-based studies

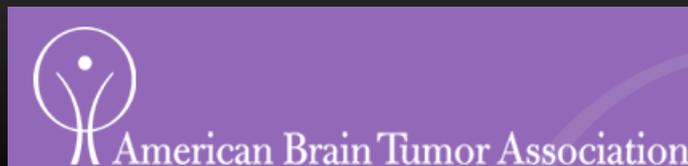
Acknowledgments

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Baylor College of Medicine

Texas Children's
The Methodist
Baylor College of Medicine



The Simmons Family



MD Anderson Cancer Center-UT

The Methodist Research Institute

Georg Speyer Haus

+ others previously mentioned

The Clayton Foundation

P01 (HEH)

Leukemia and Lymphoma SPORE

NHLBI PACT grant to Cell and Vector
Production Labs

Thank you

