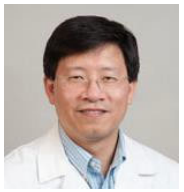
CDR3 Therapeutics Investment Prospectus

CDR3 THERAPEUTICS TEAM

(3 FOUNDER COMRADES DOING RESEARCH)

Scott G. Kitchen, PhD (Founder) - UCLA Professor of Medicine.
College: Univ Arizona, Graduate (Immunology): UCLA, Postdoc (Immunology): UCLA



Otto O. Yang, MD (Founder) – Associate Chief of Infectious Diseases at UCLA, Professor of Medicine, Microbiology, Immunology, and Molecular Genetics.
College: Brown Univ, Medical: Brown Univ, Residency (Internal Medicine): NYU-Bellevue, Fellowship/Postdoc (Infectious Diseases/Immunology): Harvard Med-Mass General

Jerome A. Zack, PhD (Founder) - UCLA Distinguished Professor of Medicine, Chair of Microbiology, Immunology, and Molecular Genetics.
College: UC Irvine, Masters (Virology): Cal State Long Beach, Graduate (Immunology): Univ Texas Health Science Center Dallas (now UT Southwestern), Postdoc (Virology): UCLA

Matthew C. Lorence, PhD, MBA (Chief Executive Officer) - College: UC Berkeley, PhD (Microbiology): Univ Texas Dallas, MBA: Univ Texas Dallas; Postdoc (Reproductive Biology); UT Southwestern Medical Center at Dallas

CANCER BREAKTHROUGH: GENETIC RETARGETING OF KILLER T CELLS

CDR3 THERAPEUTICS IMMUNITY BY DESIGN

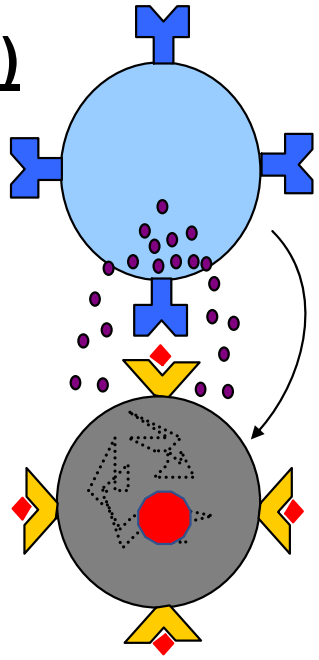
Breakthrough treatment for B cell lymphomas/leukemias: ***Retargeting killer T cells*** by genetic engineering to deliver **CARs** (CAR-T cells, Kymriah from Kite/Gilead)

Killer T Cell (CTL)

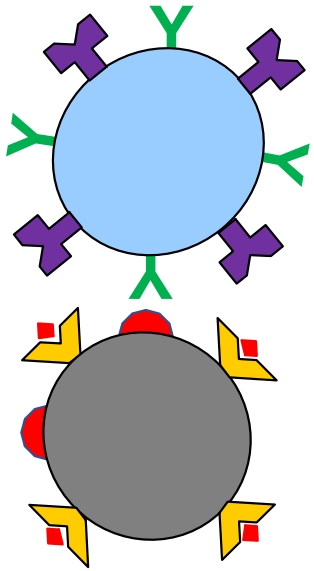
T Cell Receptor (TCR)

Release of Destructive Enzymes and Signal for Cell Death

Undesirable Cell



Artificial TCR = Chimeric Antigen Receptor (CAR)

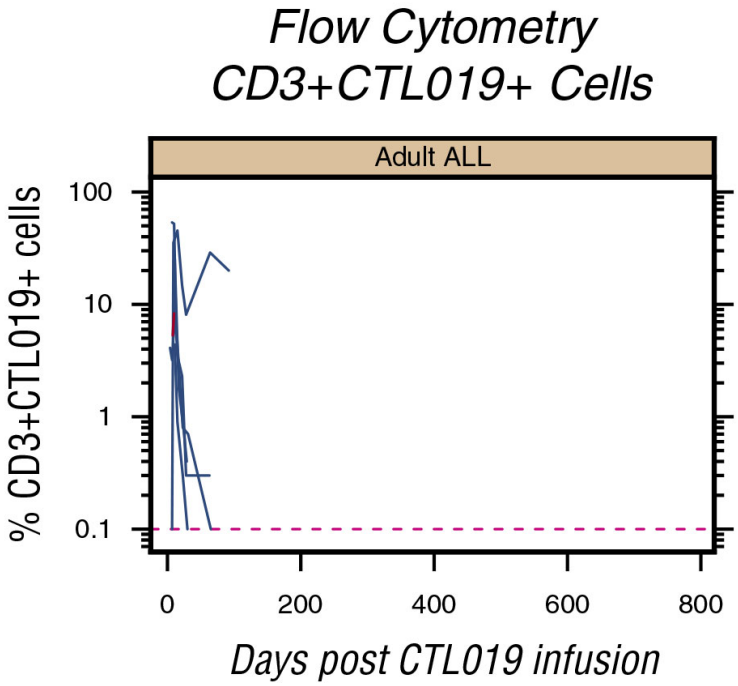


- Each CTL normally has a single TCR that determines its natural target
- Delivering a gene for another TCR or CAR can ***re-target*** a CTL as desired

T CELL GENE THERAPY: THE PROMISE BUT THE CURRENT SETBACK

CDR3 THERAPEUTICS IMMUNITY BY DESIGN

Current CAR-T cell treatment: Engineered T cells gone within weeks



From: Mueller et al, Blood, Volume 130, Issue 21, 2017, p2317-2325.
https://www.sciencedirect.com/science/article/pii/S0006497120326987

- Stalled success: Failure against solid tumors and chronic viral infections that need ***sustained*** responses
- Current method for CAR-T: ***Laboratory-expanded/processed blood T cells***

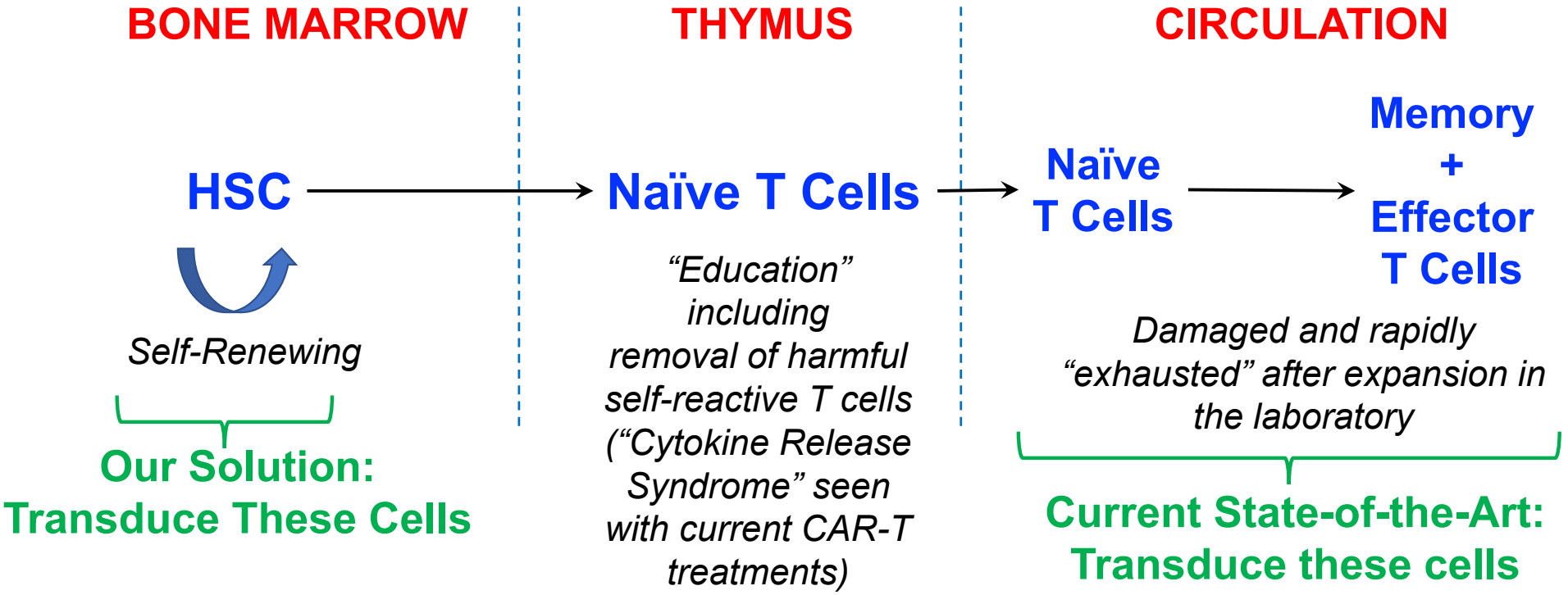
T CELL GENE THERAPY: THE PROMISE BUT THE CURRENT SETBACK

CDR3 THERAPEUTICS IMMUNITY BY DESIGN

- Current attempted solutions are downstream of the problem: Genetic modifications to ***alter the biology*** (changed death/growth pathways, genome editing to avoid immunosurveillance, also important in cancer biology) of the damaged T cells
- Our unique solution: Have the body make healthy T cells; put the retargeting gene into hematopoietic stem cells ***(HSCs)*** that create engineered T cells normally

T CELL GENE IMMUNOTHERAPY: OUR SOLUTION EMPLOY NORMAL *IN VIVO* PRODUCTION OF T CELLS

CDR3 THERAPEUTICS
IMMUNITY BY DESIGN



CURRENT T CELL GENE IMMUNOTHERAPY VS CDR3 STEM CELL GENE IMMUNOTHERAPY

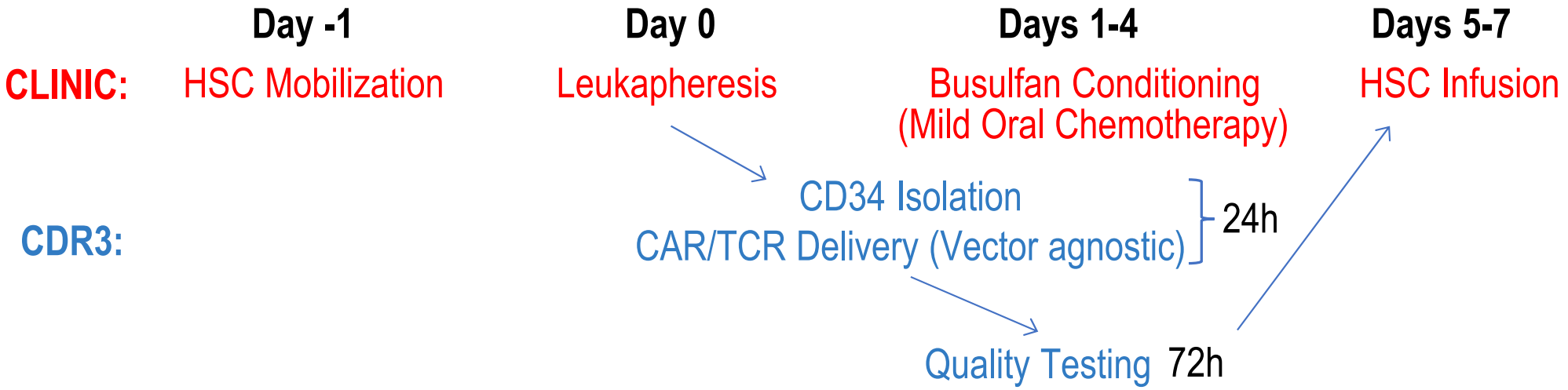
CDR3 THERAPEUTICS IMMUNITY BY DESIGN

	Current T Cell Approach	CDR3 HSC Approach
Cell Processing	Large scale laboratory expansion	No expansion
Cell Engraftment	□ Altered by *ex vivo* expansion □ Rapid death □ Limited low persistence	□ Long term engraftment □ Continuous/persistent production of healthy normal T cells *in vivo*
Lymphodepletion	Yes	No
Cell Development/ Function	□ Late stage cells □ Reduced functions (limited ability to grow, survive, distribute)	□ Normal development in the body □ Normal functions
Potential to Avoid CRS/Off-Target Effects	No	Yes (Thymic selection)

Using proprietary patented IP exclusively licensed from UCLA, CARs or TCRs are transduced into patient stem cells that engraft in the bone marrow to provide a permanent supply of functional killer T cells targeting the cancer or virus-infected cells

CDR3 STEM CELL IMMUNOTHERAPY: POTENTIALLY AN *OUTPATIENT* PROCEDURE

CDR3 THERAPEUTICS
IMMUNITY BY DESIGN



Advantages Versus Current Peripheral T Cell Therapies

- Rapid: 5-7 days versus 21-28 days
- No toxic lymphodepletion required; may avoid hospitalization
- Fewer transduced cells needed since they self-expand *in vivo* (less risk for cancer)

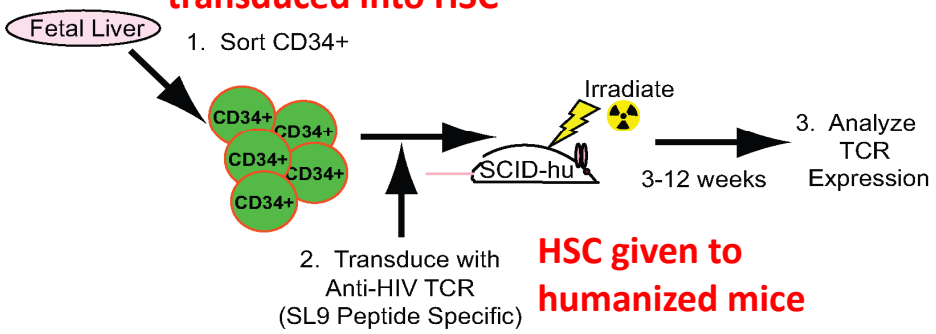
CDR3 Process Is:

- Quicker
- More Effective
- Safer
- Cheaper

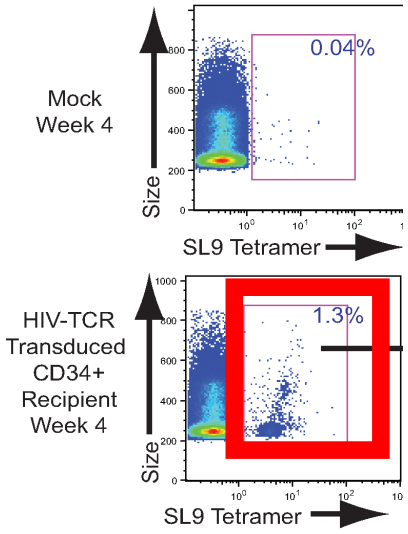
PROOF-OF-CONCEPT: HIV IMMUNOTHERAPY
HUMANIZED MOUSE MODEL TCR HSC THERAPY

CDR3 THERAPEUTICS IMMUNITY BY DESIGN

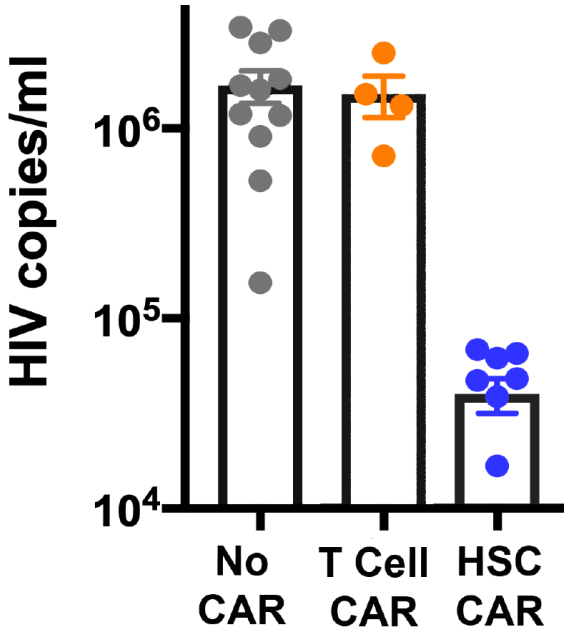
TCR against HIV transduced into HSC



HSC given to humanized mice



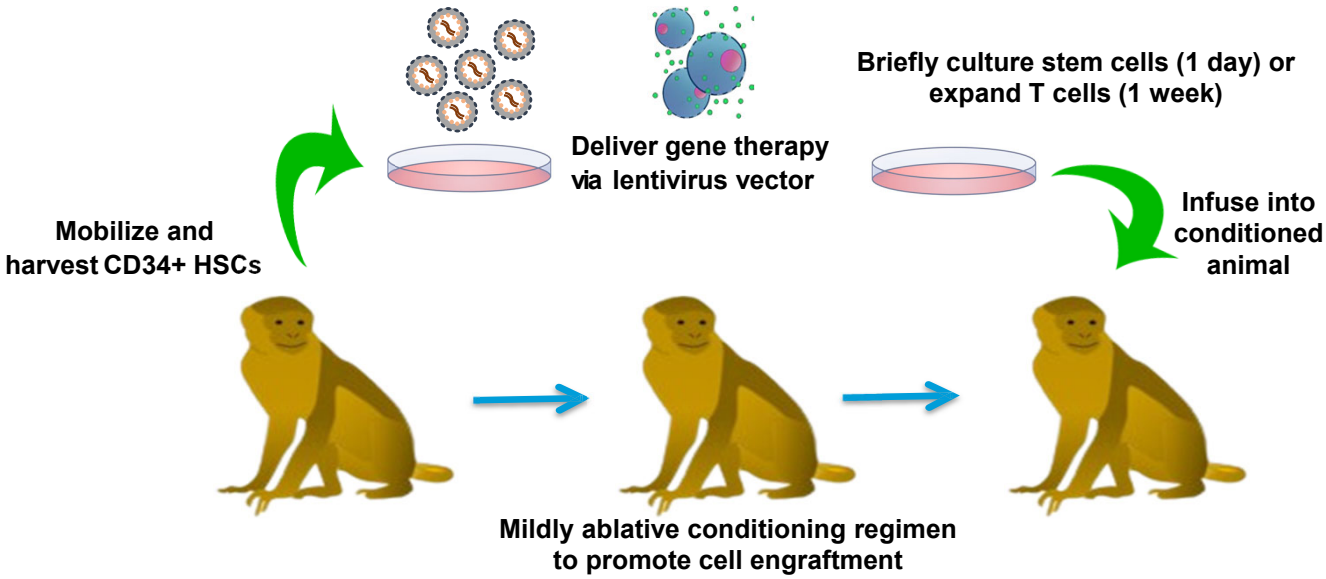
HSC develop into human T cells with the TCR



CARs delivered via HSC suppress HIV better than CARs delivered via peripheral T cells

PROOF-OF-CONCEPT: HIV CAR IMMUNOTHERAPY MACAQUE MODEL OF AIDS

CDR3 THERAPEUTICS IMMUNITY BY DESIGN



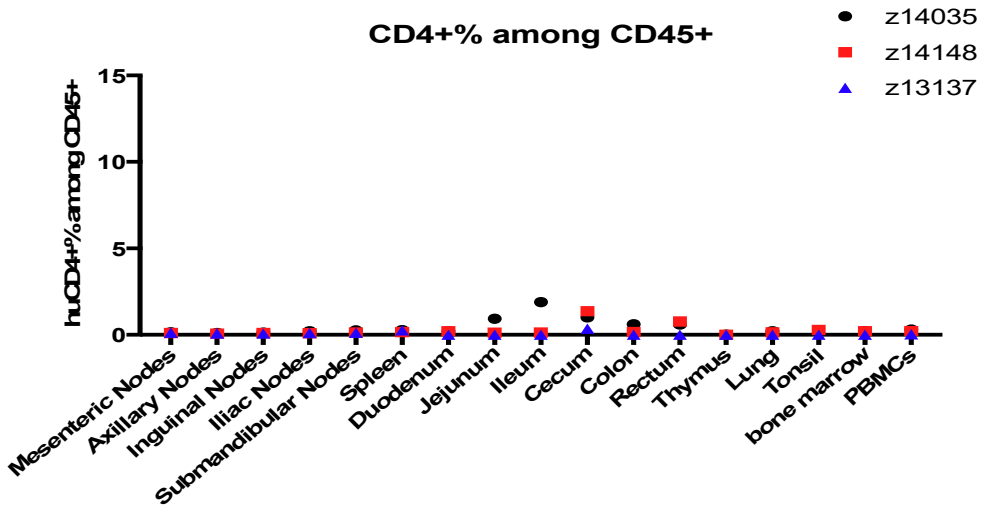
- Long-term (≥ 2 year) persistence, safe and non-toxic
- Formation of engineered T cells residing in many anatomical sites like normal T cells
- Engineered T cells reactive against HIV both in laboratory testing and reducing virus in the animals

In collaboration with Dr. Chris Peterson, Dr. Hans-Peter Kiem et al.

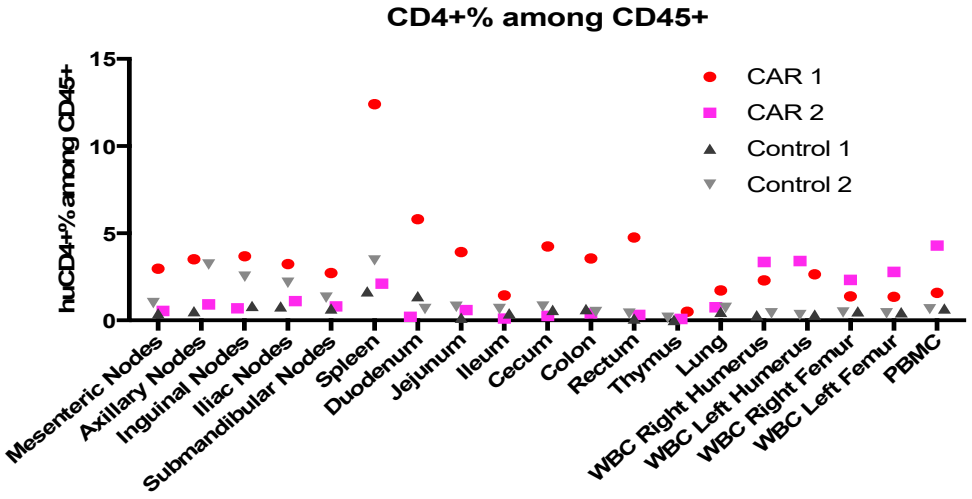
PROOF-OF-CONCEPT: HIV CAR IMMUNOTHERAPY MACAQUE MODEL OF AIDS

CDR3 THERAPEUTICS
IMMUNITY BY DESIGN

Current Technology
Delivered by Peripheral T Cells



CDR3 Approach
Delivered by HSC



Standard CAR delivery through blood T cells produces CAR-T cells that don't normally move through different body tissues, but HSCs produce healthy CAR-T that normally distribute

In collaboration with Dr. Chris Peterson, Dr. Hans-Peter Kiem et al.

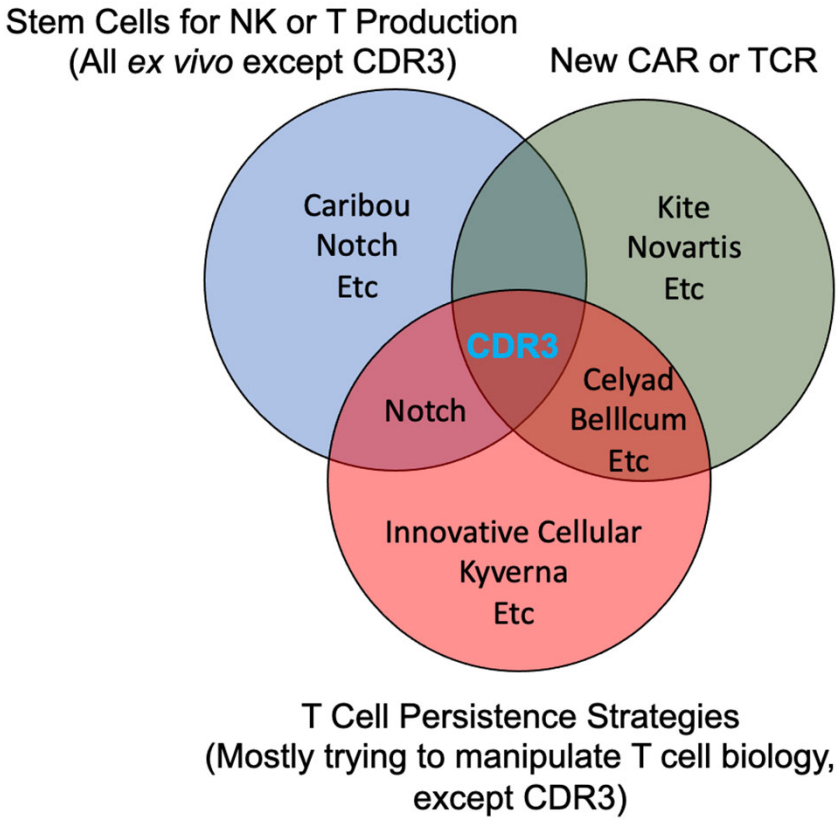
T CELL GENE IMMUNOTHERAPY: THE NEED

- Despite current limitations (only six FDA cleared CARs since 2017 against two B cell targets), the T cell gene therapy market is projected to reach ***$17.3B by 2027***

  (https://www.acumenresearchandconsulting.com/t-cell-therapy-market)

- Our technology will greatly broaden the market to include currently untreatable cancers and chronic viral infections

COMPETITORS:



- Stem cells: Other companies are not putting them into patients (just using in the lab to make other cell types)
- New CAR/TCR: Companies such as Kite are based entirely on one or a few new CARs/TCRs
- T cell persistence: Other companies are trying to alter T cells *after* they have become abnormal; only CDR3 has the body make normal T cells

BUSINESS MODEL

CDR3 THERAPEUTICS
IMMUNITY BY DESIGN

Autologous cell therapy (similar to Kite and Juno services)

- Current market price is $373K for Yescarta and $475K for Kymriah
- Patient cells processed at regional CDR3 lab and shipped to clinic
- Our current estimated net cell production cost is ~$75K/patient once scaled
- Estimated revenue at 70% GM of $250,000 per patient
- Cell processing SOP the same for all indications, differing only by receptor
- Potentially significant cost savings, especially if outpatient

INITIAL DISEASE TARGETS TO ESTABLISH OUR PLATFORM TECHNOLOGY: HPV AND CMV

CDR3 THERAPEUTICS IMMUNITY BY DESIGN

Human Papillomavirus (HPV)-associated cancers (5% of all cancers worldwide)

- Head/neck, cervical, vagina/vulvar, penile, anal, others
- $16.3 billion in 2018 and growing at a 4.5% CAGR

Cytomegalovirus (CMV)

- Benign chronic infection in most healthy people, but severe life-threatening infection in people with weakened immune systems
- “Orphan Disease” status in transplant patients ($1.2 billion in 2020, growing at a 12.3% CAGR)

HIV and other chronic viral infections (Projected to reach $44.2 billion by 2026)

- https://www.globenewswire.com/news-release/2020/02/20/1987756/0/en/Antiviral-Drugs-Market-Worth-USD-44-2-billion-by-2026-at-3-2-CAGR-Rising-Prevalence-of-HIV-to-Fuel-Growth-Fortune-Business-Insights.html
- https://www.delveinsight.com/report-store/cytomegalovirus-cmv-infection-market

PARALLEL CANDIDATES TO A HUMAN PROOF-OF-CONCEPT TRIAL: ADVANTAGES AND DISADVANTAGES

CDR3 THERAPEUTICS IMMUNITY BY DESIGN

Target Disease	TCR or CAR Available	Animal Testing Data	Orphan Disease	Disease with No Effective Treatments	Patient Already Getting HSC Transplant
Advanced HPV-Associated Cancer	No*	No*	No	**Yes**	No
CMV Prevention in Bone Marrow Transplantation	**Yes**	No**	**Yes**	No	**Yes**
HIV* **	**Yes**	**Yes**	No	No	No

** In discussion for potential licensure of a TCR that has already been in human trials with peripheral T cells*

*** In progress*

**** Proof-of-concept, potential for grant funding*

SEED ROUND FUNDING GOAL: $5M

CDR3 THERAPEUTICS
IMMUNITY BY DESIGN

- *Goal: Within two years, complete all pre-clinical development to start a phase I FDA trial for at least one disease indication that will provide proof-of-concept for our therapeutic platform*
- Convertible note
- Discount Rate 20%
- Interest 4%
- Valuation Cap $50M

PURSUING THE QUICKEST PATH TO IND FOR PROOF-OF-CONCEPT OF THE PLATFORM

CDR3 THERAPEUTICS IMMUNITY BY DESIGN

- Secure additional IP from founders' ongoing grant-funded research by exclusive licensing through UCLA
- Accelerate paths to clinical trials for **HPV-cancer** and **CMV**:
  - Production of HPV TCR for pre-clinical testing (in parallel with existing TCR license opportunity)
  - Pre-clinical animal testing of HPV TCR and CMV CAR

GOAL OF SEED FUNDING: QUICKEST PATH TO IND FOR ONE OR MORE DISEASES

CDR3 THERAPEUTICS IMMUNITY BY DESIGN

- Laboratory ”incubator space” at UCLA/CNSI to establish GMP processes ($2,500/month)
- Prodigy machine, GMP cell processing unit ($500k)
- Staff scientist for process development and NIH SBIR grant applications for non-dilutional funding ($150k/year)
- Outsourced large batch GMP vectors for both pre-clinical testing and eventual clinical trial ($300k/vector)
- Regulatory specialist for pre-IND discussions with FDA ($150k/year)

THERAPEUTIC DEVELOPMENT TIMELINE

Chronic Viral Infections

Target	Discovery	Preclinical	IND enabling	IND in effect	Phase 1	Phase 2/3
HIV			Q2-Q4 22	Q1-Q3 23	Q3 23-Q2 24	Q3 24-Q4 26
CMV		Q3 22	Q4 22-Q2 23	Q3-Q4 23	Q1-Q4 24	Q1 25-Q2 26

Virus-Associated Cancers

Target	Discovery	Preclinical	IND enabling	IND in effect	Phase 1	Phase 2/3
HPV	Q2-Q3 22	Q4 22	Q1-Q3 23	Q4 23-Q1 24	Q2 24-Q2 25	Q3 24-Q2 27

Platform IND for all future clinical trials because the patient conditioning regimen and treatment protocol is the same for all chronic viral infections and virus-associated cancers

WHAT SETS US APART

- Unique hematopoietic stem cell-based technology
- Portfolio of patented and proprietary CARs and expertise to create new CARs and TCRs against any virus or virus-associated cancer
- Founders with >75 years of combined viral immunology research experience, receiving >$100 million grant funding from NIH, California Institute for Regenerative Medicine (CIRM), and other agencies

SOME KEY PEER-REVIEWED STUDIES

Kitchen SG, Bennett, M, Galić Z, Kim J, Xu Q, Young A, Lieberman A, Joseph A, Goldstein H, Ng H, Yang O, Zack JA. (2009) **Engineering antigen-specific T cells from genetically modified human hematopoietic stem cells in immunodeficient mice**. PLoS ONE 4(12): e8208. doi:10.1371/journal.pone.0008208

Kitchen SG, Levin BR, Bristol G, Rezek V, Kim S, Aguilera-Sandoval C, Balamurugan A, Yang OO, and Zack JA (2012) **In vivo suppression of HIV by antigen specific T cell derived from engineered hematopoietic stem cells**. PLoS Pathogens 8(4): e1002649. PMCID: PMC3325196

Zhen A, Kamata M, Rezek V, Rick J, Levin B, Kasparian S, Chen ISY, Yang OO, Zack JA, and Kitchen SG. (2015) **HIV-specific Immunity Derived from Chimeric Antigen Receptor-Engineered Stem Cells**. Molecular Therapy. PMCID: PMC4817874.

Ali A, Kitchen SG, Chen IS, Ng HL, Zack JA, and Yang OO. (2016) **HIV-1-Specific Chimeric Antigen Receptors Based on Broadly-Neutralizing Antibodies**. J Virol 90(15): 6999-7006. PMCID: PMC4944295

Zhen A, Peterson CW, Carrillo MA, Reddy SS, Youn CS, Lam BB, Chang NY, Martin HA, Rick JW, Kim J, Neel NC, Rezek VK, Kamata M, Chen ISY, Zack JA, Kiem H-P, and Kitchen SG. (2017) **Long-term persistence and function of Hematopoietic Stem Cell-derived Chimeric Antigen Receptor T cells in a Nonhuman Primate Model of HIV/AIDS**. PLOS Pathogens, Dec 28;13(12):e1006753. PMCID: PMC5746250

Barber-Axthelm, I., Barber-Axthelm, V., Sze, K-Y., Zhen, A., Suryawanshi, G.W., Chen, I.S.Y., Zack, J.A., Kitchen, S.G., Kiem, H-P., Peterson, C. (2020) **Stem cell-derived CAR-T cells traffic to HIV reservoirs in macaques**. JCI Insight, Jan 11;6(1):e141502. doi: 10.1172/jci.insight.141502. PMCID: PMC7821595

Zhen, A., Carrillo, M., Mua, W., Rezek, V., Martin, H., Hamid, P., Chen, I.S.Y., Yang, O.O., Zack. J.A., and Kitchen, S.G. (2021) **Robust CAR-T Memory Formation and Function Via Hematopoietic Stem Cell Delivery**, PLoS Pathogens, 2021 Apr 1;17(4): e1009404. https://doi.org/10.1371/journal.ppat.1009404. PMCID: PMC8016106