UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported):
February 24, 2021

Poseida Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-39376**	**47-2846548**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

9390 Towne Centre Drive, Suite 200
San Diego, California **92121**
(Address of principal executive offices) **(Zip Code)**

Registrant's telephone number, including area code: (858) 779-3100

N/A
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.0001 per share	**PSTX**	**Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b–2 of the Securities Exchange Act of 1934 (§ 240.12b–2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On February 24, 2021, members of management of Poseida Therapeutics, Inc. (the "Company") and external advisors are providing an update on the Company's research and development programs and making available the presentation attached as Exhibit 99.1 to this report. The presentation is also available under the "Investors" section of the Company's website.

The information in this Item 7.01 of this report (including Exhibit 99.1) is furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information shall not be deemed incorporated by reference into any other filing with the Securities and Exchange Commission made by the Company, whether made before or after today's date, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific references in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate presentation, dated February 24, 2021

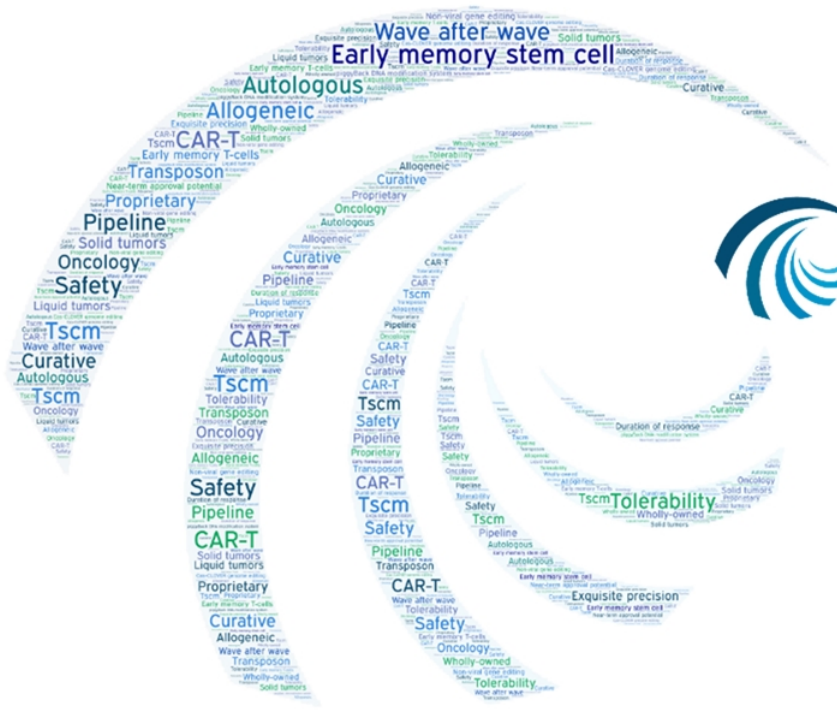
SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Poseida Therapeutics, Inc.

Date: February 24, 2021

By: /s/ Harry J. Leonhardt
Harry J. Leonhardt
General Counsel and Chief Compliance Officer



POSEIDA THERAPEUTICS

The Next Generation of Cell and Gene Therapeutics with the Capacity to Cure

R & D Day

February 24, 2021

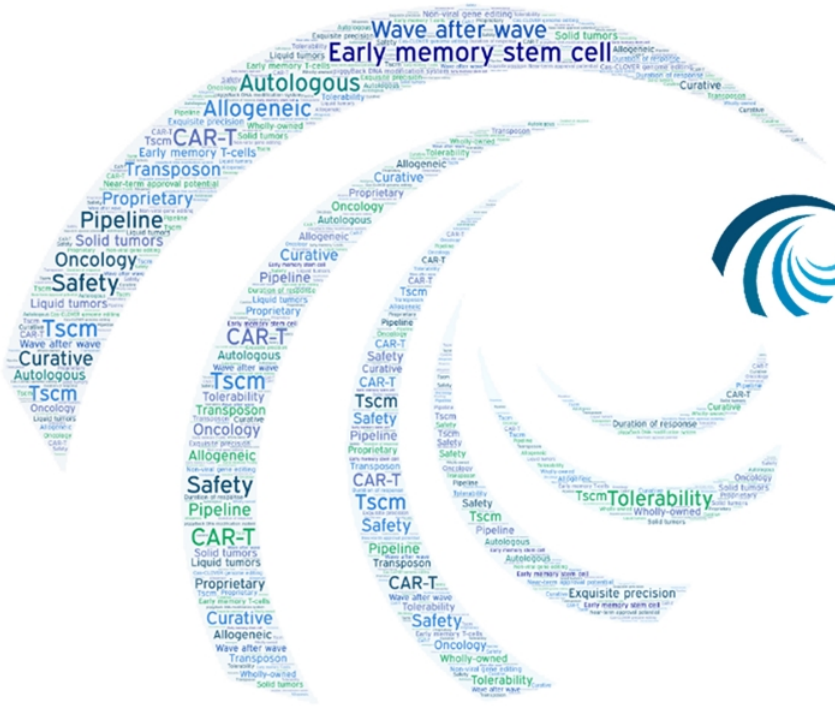
Disclaimer

This presentation and any accompanying oral commentary contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts and include, without limitation, statements related to future events; our future financial performance or condition; business strategy; expected timing and plans with respect to development milestones, clinical trials, and regulatory activities; estimated market opportunities for product candidates; and future results of anticipated development efforts. Words such as "expect(s)," "feel(s)," "believe(s)," "will," "may," "anticipate(s)", “potentially” or negative of these terms or similar expressions are intended to identify forward-looking statements. These forward-looking statements are based on management's current expectations of future events only as of the date of this presentation and are subject to a number of important risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: risks associated with conducting clinical trials; whether any of our product candidates will be shown to be safe and effective; our ability to finance continued operations; our reliance on third parties for various aspects of our business; competition in our target markets; our ability to protect our intellectual property; our ability to retain key scientific or management personnel; and other risks and uncertainties described in our filings with the Securities and Exchange Commission, including under the heading “Risk Factors”. Except as required by law, we assume no obligation to update these forward-looking statements, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

R&D Day Agenda

Select Poseida Programs and Technologies

- Corporate Overview (Eric Ostertag, CEO)
- Cell and Gene engineering platform technologies
  - Super PiggyBac DNA Modification System for Gene Insertion
  - CAS-CLOVER + Gene Editing
  - Gene Delivery
  - Proprietary Tools
- Immuno-oncology Programs, Analysis & Updates
  - Clinical Programs (Matt Spear)
  - Selected Pre-clinical Programs (Blair Madison, Devon Shedlock)
- Gene therapy Introduction + Pipeline
  - Initial focus: liver directed gene therapies
    - piggyBac + AAV (Bruce Scharschmidt)
    - P-OTC-101
  - piggyBac + nanoparticle (Denise Sabatino)
    - Hemophilia - Factor VIII
- Emerging Discovery Programs
  - TCR-T Platform (Sumiti Jain)
  - CAR-T Outside Oncology (Nina Timberlake)
  - HSC Platform (Claire Koechlein)
  - CAR-NK Cells for oncology (Stacey Kranert)
- Conclusion
  - Business development / partnership strategy
  - Long-term Goals/Mission
- Closing Q&A



POSEIDA THERAPEUTICS

R&D Day

Eric Ostertag, M.D., Ph.D.
CEO and Founder

Poseida Therapeutics, Inc.

Introduction to Poseida Therapeutics

Company Snapshot

NASDAQ: PSTX
IPO in July 2020

High-Quality
Shareholder Base

Spin out of **Transposagen Biopharmaceuticals** in 2015

Strong and **Broad IP** Portfolio

Headquartered in **San Diego, CA**

~200
Employees

Presenters

Eric Ostertag, M.D., Ph.D.
Chief Executive Officer

Matt Spear, M.D.
Chief Medical Officer

Denise Sabatino, Ph.D.
University of Pennsylvania
Children's Hospital of Philadelphia

Bruce Scharschmidt, M.D.
Consultant / P-OTC-101 Program Lead

Stacey Cranert, Ph.D.
Associate Director, Research

Mark Gergen
President & Chief Business Officer

Devon Shedlock, Ph.D.
SVP, Research and Development

Sumiti Jain, Ph.D.
Director, Research Immuno-oncology

Renata Martin, Ph.D.
Research Scientist
Genetic Engineering

Claire Koechlein, Ph.D.
Associate Director
Research Scientific Evaluation

Nina Timberlake, Ph.D.
Associate Director, Research

Blair Madison, Ph.D.
Senior Director
Genetic Engineering

Cell and Gene Engineering Platform Technologies

POSEIDA THERAPEUTICS

Poseida Therapeutics

Powerful Platforms and Products to Drive Value Creation

- **Innovative technology platforms** enable broad **cell and gene therapy** pipeline and beyond
- Differentiated **autologous and allogeneic CAR-T** programs
  - **Stem cell memory T cells (T_{SCM})** drive superior product profile
  - Iterative pipeline approach with **multiple shots on goal**
    - **BCMA** programs targeting **multiple myeloma**
    - **PSMA and MUC1C** programs addressing **multiple solid tumor** indications
      - **prostate, ovarian, breast and more**
    - **Dual CAR programs** that promise to take CAR-T to the next frontier
- Novel **Gene Therapy** programs aimed at single treatment cures for rare diseases
  - **piggyBac** technology can enable **single-treatment cures**
  - **Novel nanoparticle** technology can **eliminate limitations of AAV**
- Significant opportunities for **partnership, collaboration and platform expansion** beyond current pipeline

Platform Driven Cell and Gene Therapy Company Creating Value Through Innovation and Differentiated Patient Therapies

Poseida's Novel Approach to Cell and Gene Therapeutics

GENE INSERTION

Super piggyBac

- Non-viral system
- Highly efficient technology to add DNA to genome
- Large genetic cargo capacity
- Broad range of cells
- Advantages in tolerability, potency, speed to clinic and costs

GENE EDITING

Cas-CLOVER
TAL-CLOVER

- Highly precise site-specific nucleases
- Ability to edit resting T cells while maintaining desirable T_{SCM} characteristics
- Major advantages:
  - tolerability
  - ease of design
  - low cost
  - multiplexing ability

GENE DELIVERY

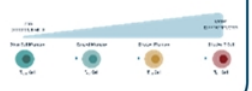
Nanoparticles
AAV Vectors

- Delivers long-term stable gene expression
- Non-viral and viral delivery of DNA and proteins both ex vivo and in vivo
- Ability to deliver to multiple cell types and target specific tissues

CAR-T TOOLS

T_{SCM} production platform
Booster molecule

- Ability to produce nearly pure CAR-T+ cells with high percentage of T_{SCM} phenotype
- Booster molecules enable manufacturing of hundreds of doses from single run



Proprietary and Highly Differentiated Technologies in a Competitive Cell and Gene Therapy Space

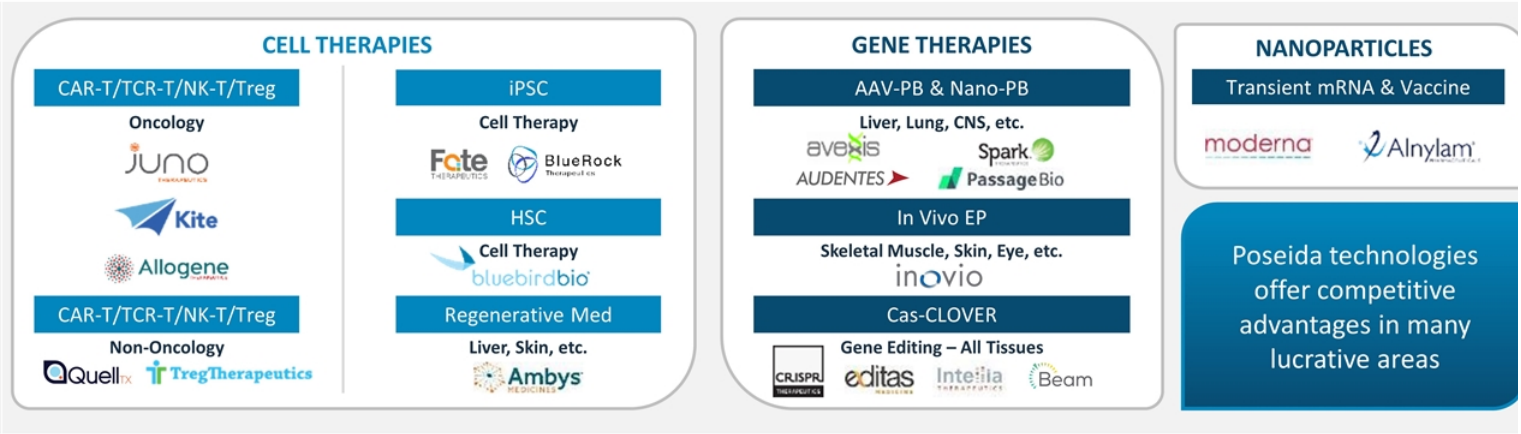
POSEIDA THERAPEUTICS

Platform Technologies Can Be Combined in Various Ways to Drive Significant Value in Multiple Market Segments

piggyBac
DNA Modification System

Cas-CLOVER
Gene Editing System

Nanoparticle/AAV
Delivery Technology



Super piggyBac®
Gene Delivery System

POSEIDA THERAPEUTICS

Poseida's Novel Approach to Cell and Gene Therapeutics

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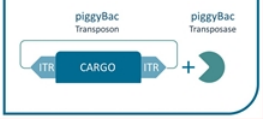

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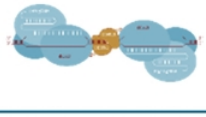

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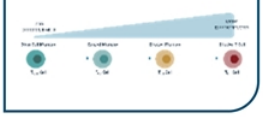
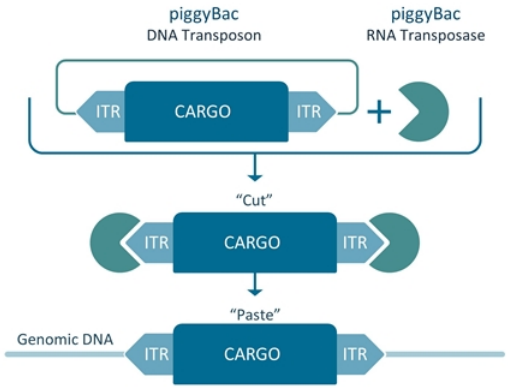


Proprietary and Highly Differentiated Technologies in a Competitive Cell and Gene Therapy Space

POSEIDA THERAPEUTICS

piggyBac®: A Versatile DNA Delivery System for Developing Cell and Gene Therapy Products



- Non-viral gene insertion technology
- Enables DNA integration and stable expression
- Very large cargo capacity (~200 kB)
- Works in a wide variety of cell types
- Multiple safety and cost benefits

BENEFITS IN CELL THERAPY

Generating CAR-T Products with Desirable High Percentage of T_{SCM} Cells

- Preferentially favors **stem cell memory T cells (T_{SCM})** and works well in **resting T cells** for potentially improved tolerability and more durable responses
- **Large cargo capacity** enables multi-CAR products, addition of safety switch and selection gene

BENEFITS IN GENE THERAPY

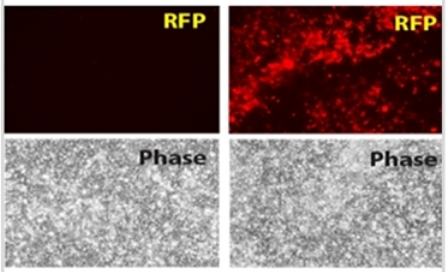
Integrates Into DNA Delivering Stable Long-Term Expression

- Ideal for use in **dividing tissues** like those in juvenile liver
- **Highly efficient** integration may allow **reduced dosing and single treatment cures**
- **Large cargo** for delivering larger genes
- **Delivered using AAV or nanoparticle** or in vivo EP

POSEIDA THERAPEUTICS

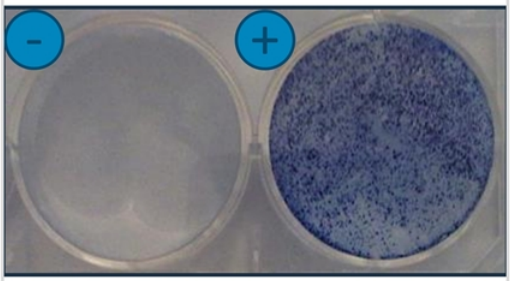
PiggyBac® is the Most Efficient Technology for Stable Delivery of DNA into the Genome in Most Cell Types

-piggyBac® Transposase | +piggyBac® Transposase



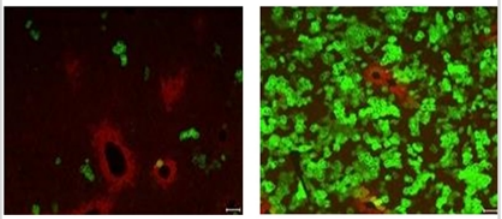
Lipofection – ex vivo (Immortalized Cells)

-piggyBac® Transposase | +piggyBac® Transposase



Electroporation – ex vivo (e.g., Stem Cells & T cells)

-piggyBac® Transposase | +piggyBac® Transposase

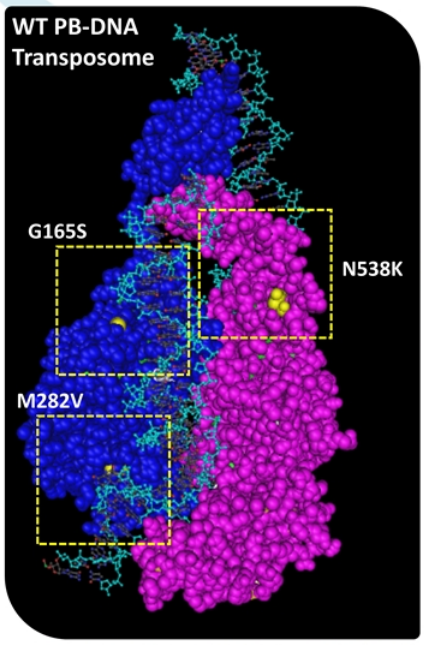


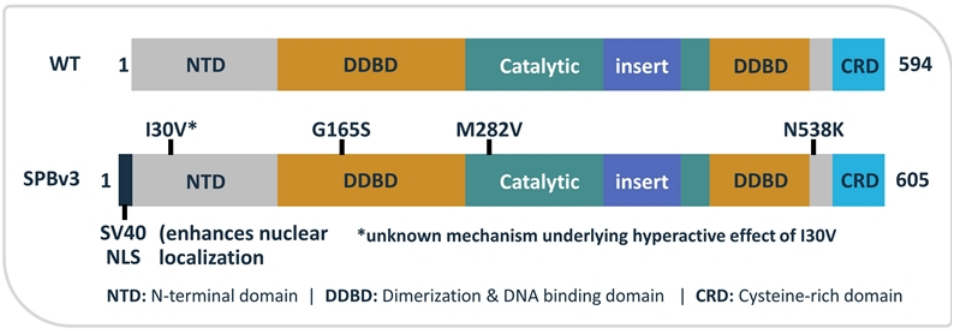
Infection or Nanoparticle – in vivo (e.g., hepatocytes)

PB delivers transgenes stably into the genome regardless of delivery vehicle

POSEIDA THERAPEUTICS

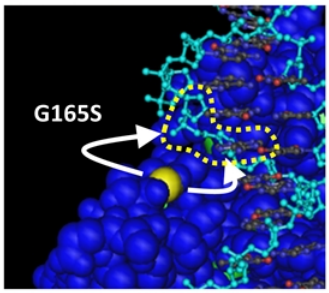
piggyBac®: WT vs. SPB





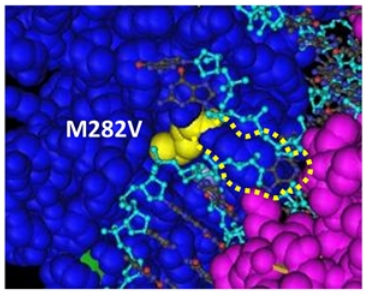
DNA-Binding

G165S: Enhances DNA binding (H-bonds w/ PO4 and Adenine)



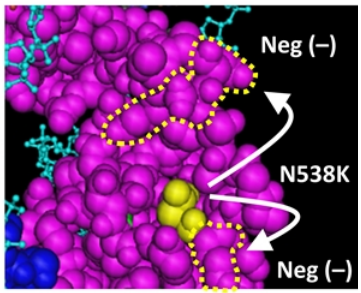
Catalysis

M282V: Enhances pi-stacking b/t Tyr283 and Adenine in TTAA



Stabilization

N538K: Electrostatic stabilization in linker between DDBD and CRD



Structure from **Chen et al.** ***Nat Commun*****, 2020 Jul 10;11(1):3446**

Hyperactive mutations from **Yusa et al.** ***PNAS, 2011 Jan 25;108(4):1531-6***

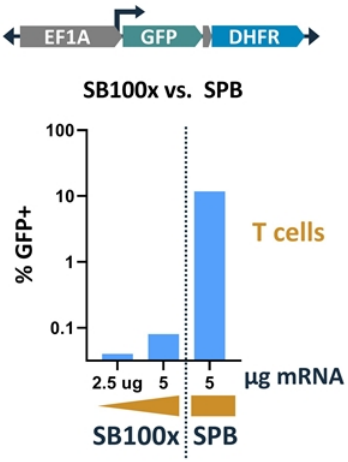
POSEIDA THERAPEUTICS

piggyBac® Best-in-class DNA Delivery System

Comparison of Technologies that Integrate into DNA

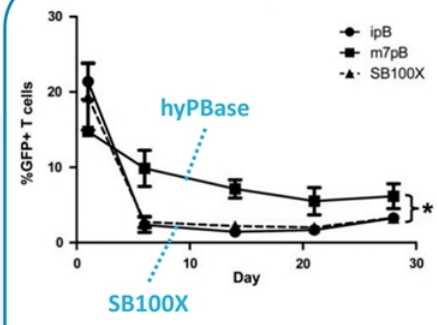
	Characteristic	Retrovirus / Lentivirus	Sleeping Beauty	piggyBac®
EFFICACY	Composition	Viral	Non-viral	Non-viral
	Insertion Efficiency	High	Medium	High
	Transgene Expression Level	High	Low	High
	Transgene Expression Stability	Medium	Medium	High
	Cargo Limit	~10-20kB	>100kB	>200 kB
	Insertion Preference	5' End of Genes / Intragenic	Random	Open Chromatin
SAFETY	Mutagenesis when Excising	N/A	Yes	No
	Effect on Local Genes	High (activator)	???	Low (insulator)
	Fully Reversible	No	No	Yes (PBx enzyme)
SPEED	Time to Clinic (CMC)	8-12 months	1-2 months	1-2 months
COST	Cost of Production	High	Low	10x Lower GMP

Super piggyBac® is the Best-in-Class Transposon System



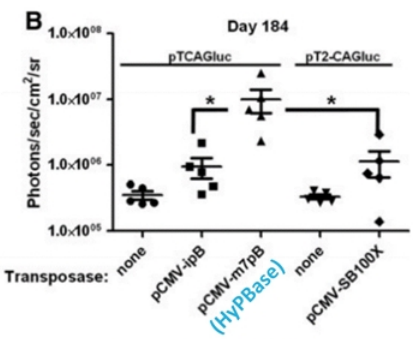
SB100x vs. SPB in Poseida Process (>100-fold better)

SB100x vs. HyPBase



T cells

SB100x vs. HyPBase



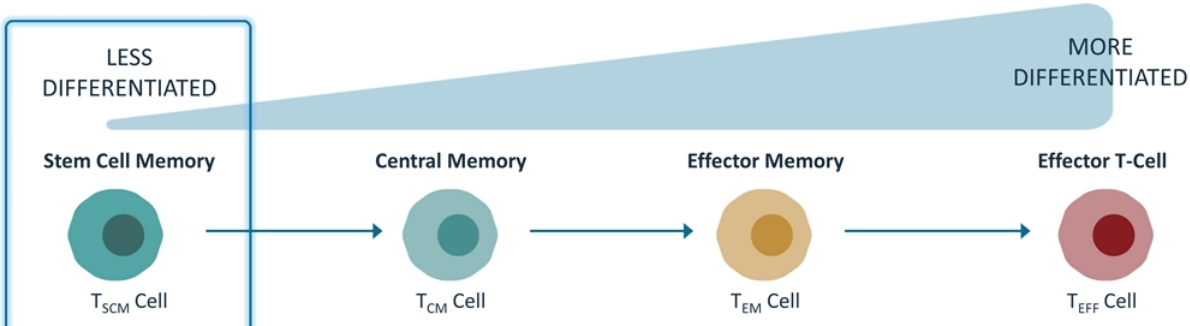
Hydrodynamic Tail Vein Inj. & BLI

Doherty et al., *HUMAN GENE THERAPY* 23:311–320 (2012)
hyPBase= I30V;S103P;G165S;M282V;S509G;N538K;N571S
SPB= I30V;G165S;M282V;N538K

POSEIDA THERAPEUTICS

Not All T-Cells are Created Equally

The Importance of Stem Cell Memory T Cells (Tscm)



- Self renewing
- Long lived
- Multipotent

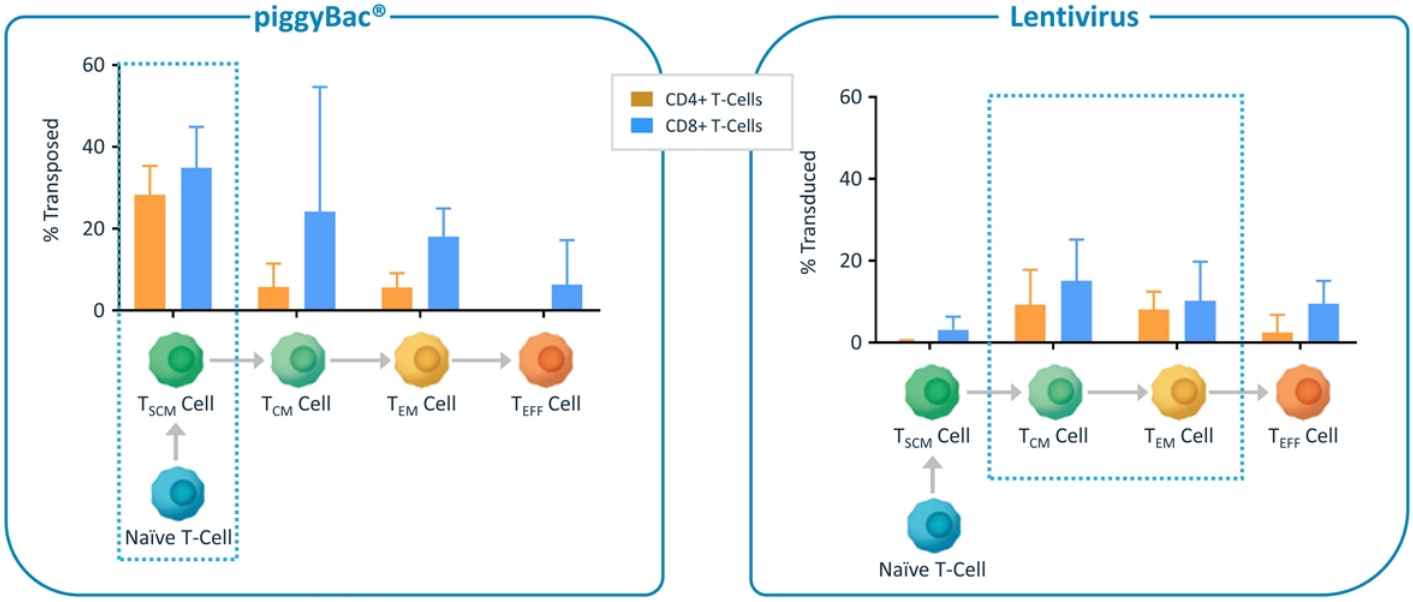
piggyBac
Designed to Preferentially Transpose T_{SCM} Cells

STEMNESS MATTERS

Products with High % of T_{SCM} Cells:

- Strong correlation with best responses in the clinic
- More gradual tumor killing with less toxicity
- Better duration of response and potential for re-response
- Key to CAR-T success in solid tumors

piggyBac® Preferentially Transposes *Early* T_{SCM} Cells; Lentivirus Transduces *More Differentiated* T-Cells In Preclinical Studies



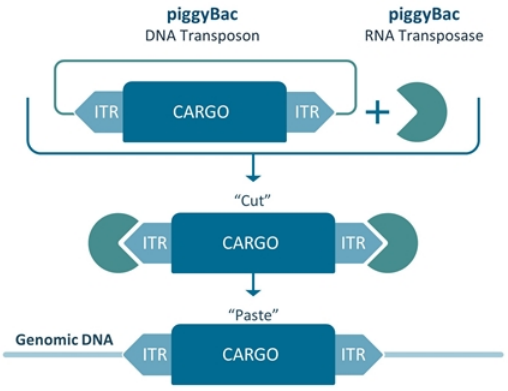
We purified donor cells to these T-cell subsets and then performed optimized piggyBac or optimized lentivirus manufacturing on each subset

Percentage transposed (% GFP+) data are displayed for CD4+ T cells (CD3+CD4+CD8-) or CD8+ T cells (CD3+CD4+CD8+) within the final cell product

POSEIDA THERAPEUTICS

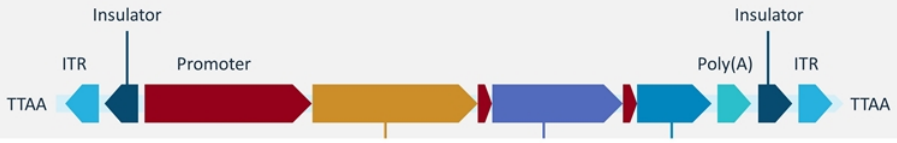
piggyBac's Cargo Capacity May Allow for Desirable Product Attributes

Very Large Cargo Capacity:
Potentially >20x Lentivirus



Large transgene with ability to carry multiple CAR or TCR molecule genes and armoring technology

Designed To Have Desirable Product Attributes



INCORPORATES PROPRIETARY SAFETY SWITCH

- Rapid, dose-dependent **elimination** of engineered T- cells as needed
- Potential **management of** Cytokine Release Syndrome (**CRS**) or other AEs

DIFFERENTIATED BINDING CAR-T MOLECULE

- VH or Centyrin™ molecule with **high-specificity binding**
- Fully human with no **tonic signaling observed to date**

DRUG RESISTANCE GENE PERMITS POSITIVE SELECTION

- **~100% of T-cells** in final product express the CAR molecule
- Predicted to result in **greater therapeutic index**

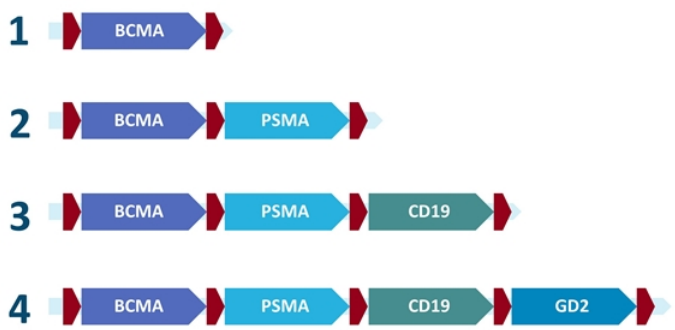
POSEIDA THERAPEUTICS

Beyond Single Target CAR-T

piggyBac® Unmatched Cargo Capacity Increases Optionality

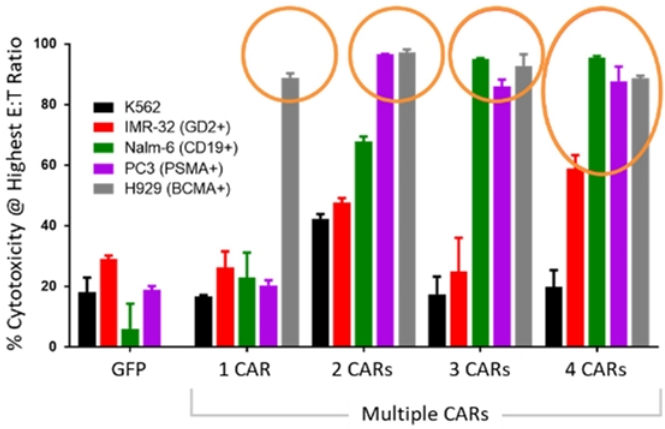
piggyBac® Can Effectively Deliver Multiple Full-length CARs or TCRs in Single Transposon System

FULL-LENGTH CARs*



** Plus selection gene and marker gene*

FUNCTION (KILLING)



POSEIDA THERAPEUTICS

Cas-CLOVER™ Site-Specific Gene Editing System

POSEIDA THERAPEUTICS

Poseida's Novel Approach to Cell and Gene Therapeutics

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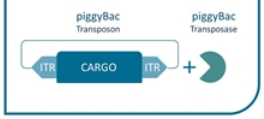

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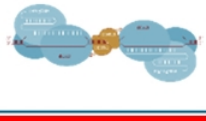
  - ease of design
  - low cost
  - multiplexing ability



GENE DELIVERY

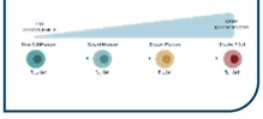
Nanoparticles
AAV Vectors

- Delivers long-term stable gene expression
- Non-viral and viral delivery of DNA and proteins both ex vivo and in vivo
- Ability to deliver to multiple cell types and target specific tissues

CAR-T TOOLS

T_{SCM} production platform
Booster molecule

- Ability to produce nearly pure CAR-T+ cells with high percentage of T_{SCM} phenotype
- Booster molecules enable manufacturing of hundreds of doses from single run



Proprietary and Highly Differentiated Technologies in a Competitive Cell and Gene Therapy Space

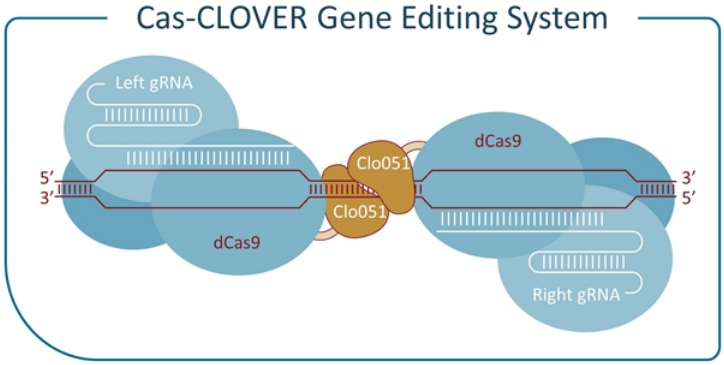
POSEIDA THERAPEUTICS

Cas-CLOVER: Proprietary Hybrid Gene Editing Platform

Potentially The Cleanest Gene Editing System Available

CRISPR/ Cas9

TALEN/ ZFN



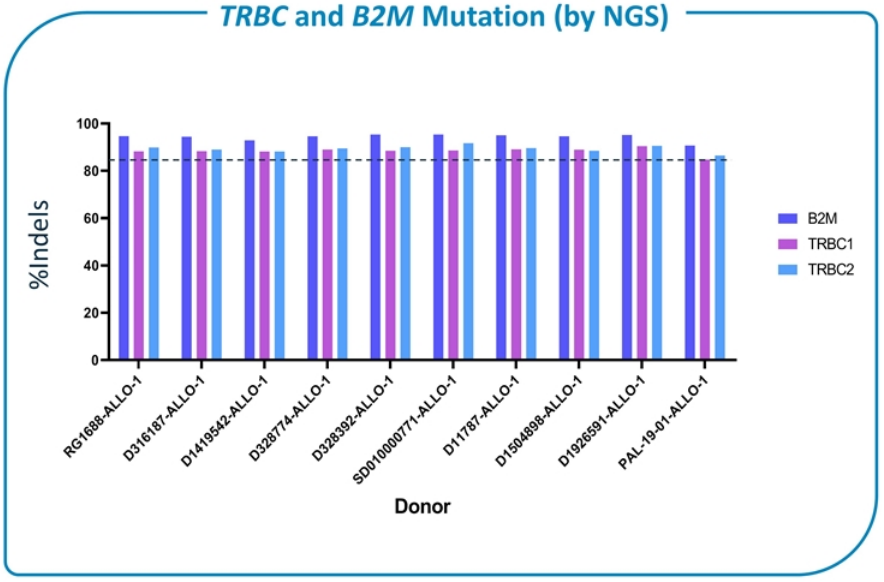
Cas-CLOVER BENEFITS

- **Low-to-no off-target cutting**
- **High Editing Efficiency** in resting T-cells resulting in high % of T_{SCM} cells
- Ease of use/design
- Multiplexing ability
- High specificity
- Lower cost

Clean, efficient and versatile gene editing platform
enables differentiated fully **Allogeneic CAR-T** products and **Gene Therapy** development

Highly Efficient ON-target Knock-out in the P-BCMA-ALLO1 Product, at Both TRBC and B2M Sites by Cas-CLOVER™

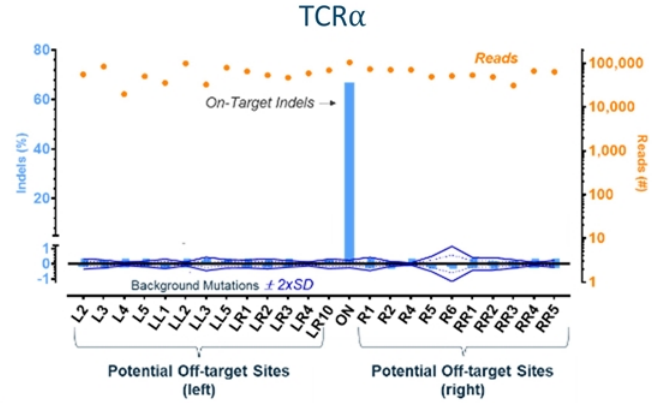
- Multiple products (10) were tested by NGS to determine editing (% Indels) at the *TRBC*1, *TRBC*2 and *B2M* sites
- Single step multiplexed editing is highly efficient: Editing at *B2M* and *TRBC* is >85% across multiple donors (by NGS)
- Functional protein knock-out confirmed by FACS, other functional assays

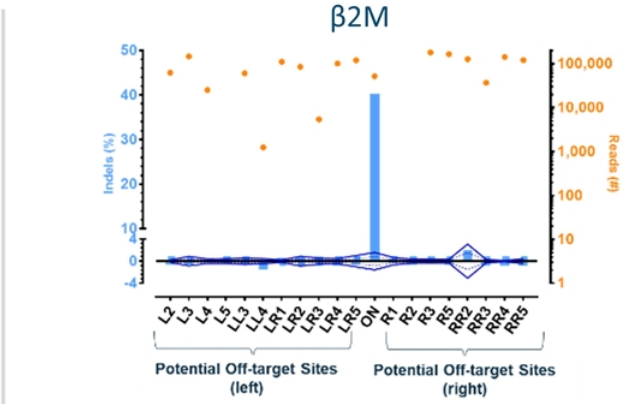


POSEIDA THERAPEUTICS

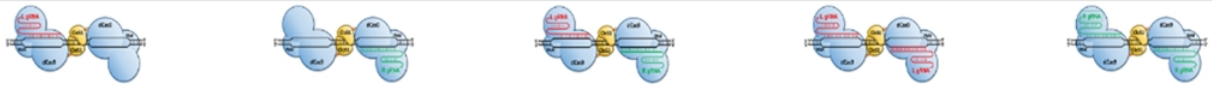
Cas-CLOVER™ is Highly Precise with No Off-Target Cutting

Data from Millions of Sequence Reads Demonstrate that CAS-CLOVER Does Not Cause Off Target Cutting





KBIOBOX



gRNA	L	R	LR	LL	RR

Data presented at ASH 2017

POSEIDA THERAPEUTICS

Nanoparticles

POSEIDA THERAPEUTICS

Poseida's Novel Approach to Cell and Gene Therapeutics

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Super piggyBac

- Non-viral system
- Highly efficient technology to add DNA to genome
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- Broad range of cells
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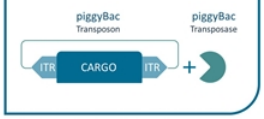

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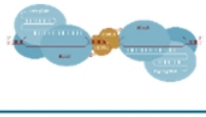

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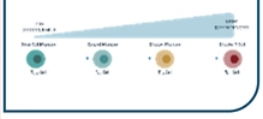


Proprietary and Highly Differentiated Technologies in a Competitive Cell and Gene Therapy Space

POSEIDA THERAPEUTICS

Delivery Platforms Enable Multiple Gene Therapy Approaches

Developing Both AAV and Non-Viral Nanoparticle Delivery

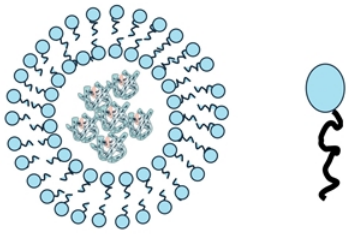
OUR GOAL:

Develop Single Treatment Cures Utilizing Our In Vivo Gene Therapy Technologies

Nanotechnology Overview

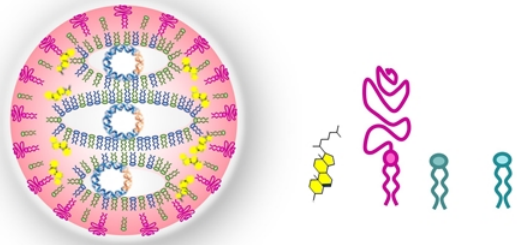
Poseida has Developed Multiple Nanoparticle Approaches

Polymersomes



- Single-component nanoparticle composed of novel block co-polymers
- Encapsulation of large, complex macromolecules (protein, plasmid DNA)
- Myoglobin delivery (PEM) may be synergistic with CAR-T

Lipidoid Nanoparticles (LNP)

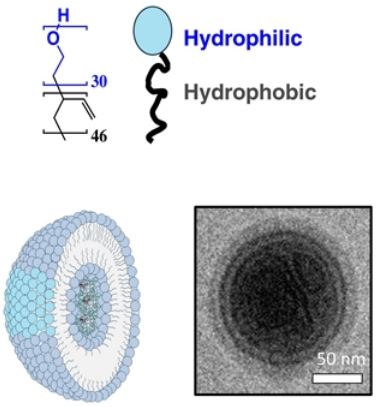


- Multi-component nanoparticle composed of known and novel lipids
- Encapsulation of nucleic acids (mRNA, DNA) for delivery ex vivo and to hepatocytes in vivo
- Editing and transposition, in vivo and ex vivo

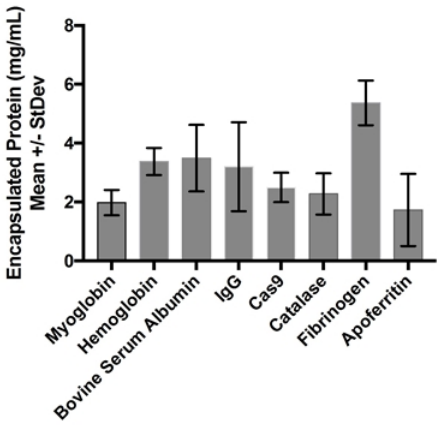
Polymersome Technology for Protein Delivery

Potential Use with CAR-T in Solid Tumors

Polymersome Structure

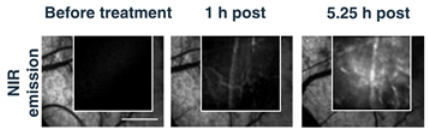


Protein Encapsulation

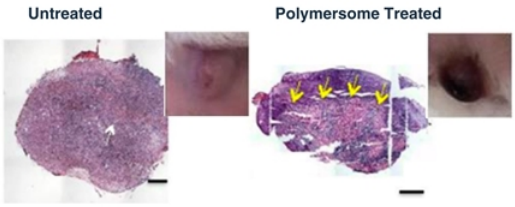


Robust encapsulation of a wide variety of proteins in polymersome

Myoglobin Delivery



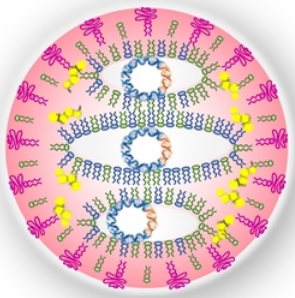
Polymersomes accumulate in tumor



Destruction of vasculature in tumor core

POSEIDA THERAPEUTICS

Lipidoid Nanoparticle Technology for Nucleic Acid Delivery

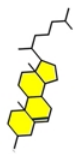


Lipidoid nanoparticle encapsulating nucleic acid

Cargo

Nucleic acid

Helper Lipids



Cholesterol

PEG-lipid

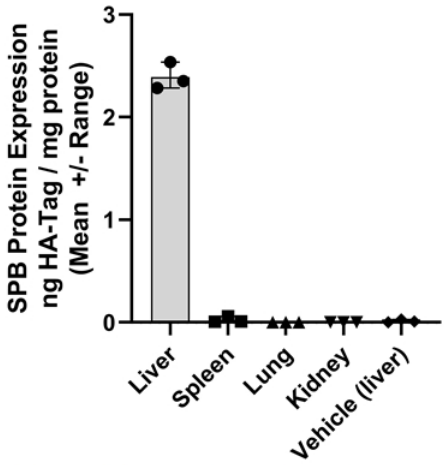
Structural lipid

Cationic Lipid

Cationic lipid

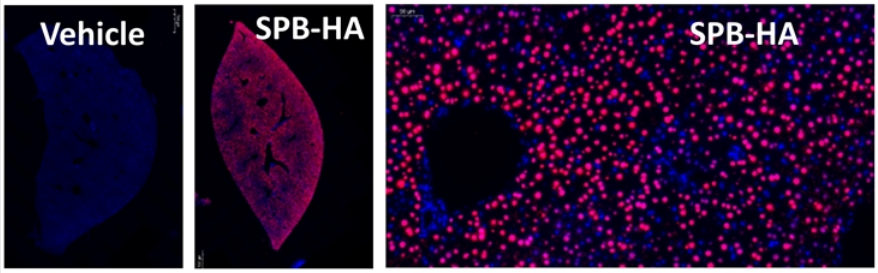
mRNA Nanoparticle for Liver-specific SPB Protein Expression

ELISA



- Minimal expression in the spleen and no detectible signal in lung and kidney
- Liver specificity was greater than for other LNP compositions evaluated to date

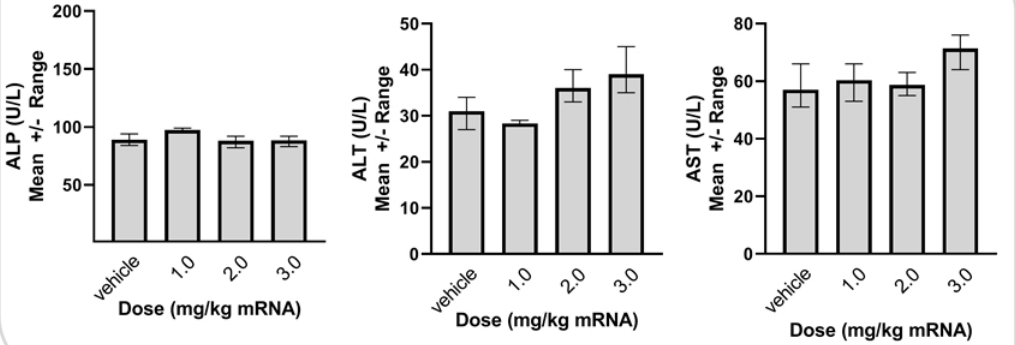
Immunofluorescence



- Homogeneous expression of SPB protein throughout liver, 4 hours post-LNP mRNA treatment

POSEIDA THERAPEUTICS

Representative Biodegradable Formulation is Well Tolerated

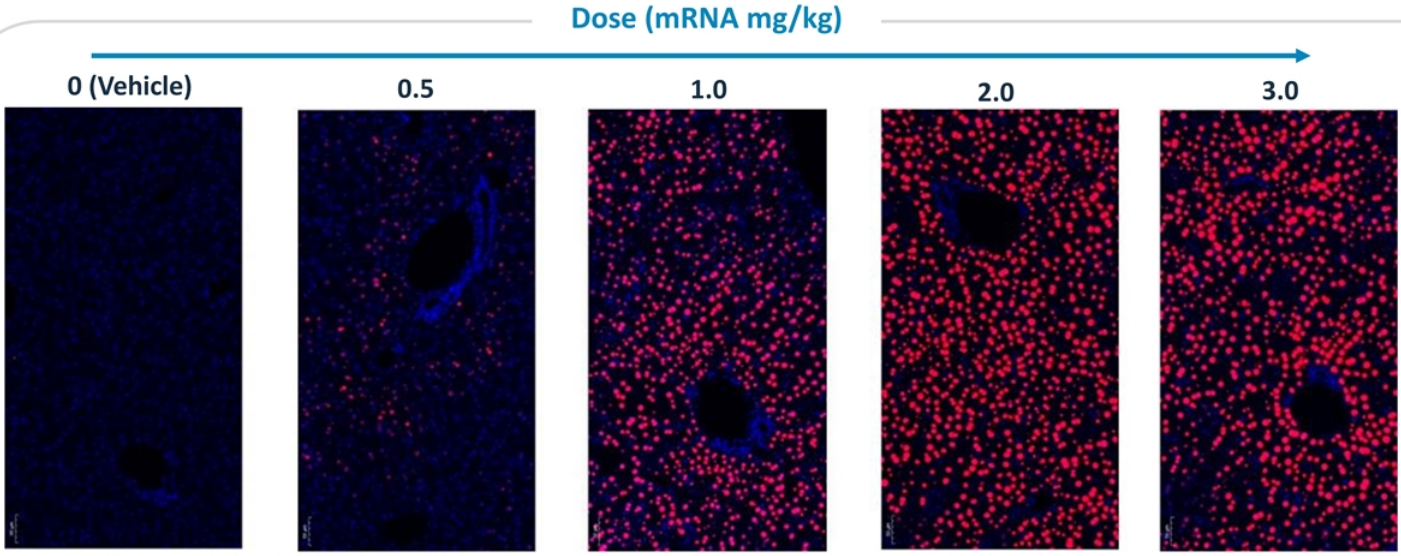


- Representative data for one Poseida formulation utilizing a biodegradable lipid
- Liver enzymes 24h after dosing
- Negligible increases at highest dose evaluated

POSEIDA THERAPEUTICS

Transposase Expression is Dose Dependent

Higher Doses May Not be Needed – But Provide Development Flexibility

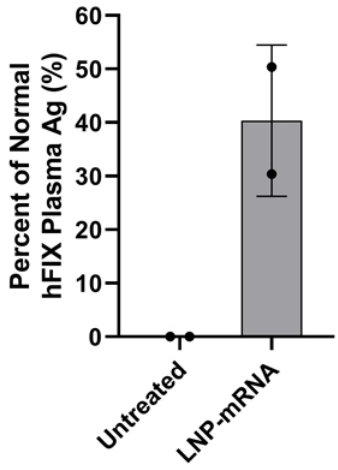


Immunfluorescence staining (X20) of SPB transposase expression (red) with DAPI counterstain (blue) in adult mouse liver 4h after IV administration of mRNA LNP

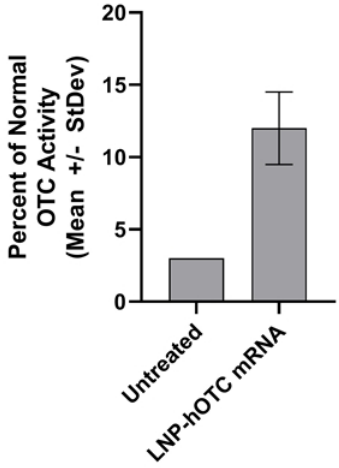
LNP for Delivery of Therapeutic mRNA

Data Demonstrate Best-In-Class RNA Delivery

Factor IX mRNA in adult BALB/C mice

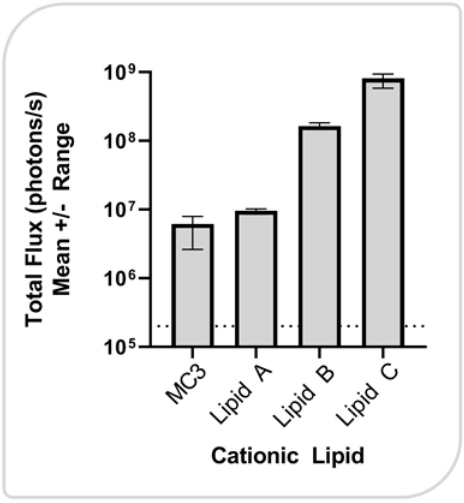


OTC mRNA in adult SPF-Ash mice



DNA Nanoparticles Demonstrate Superior Efficacy Compared to MC3

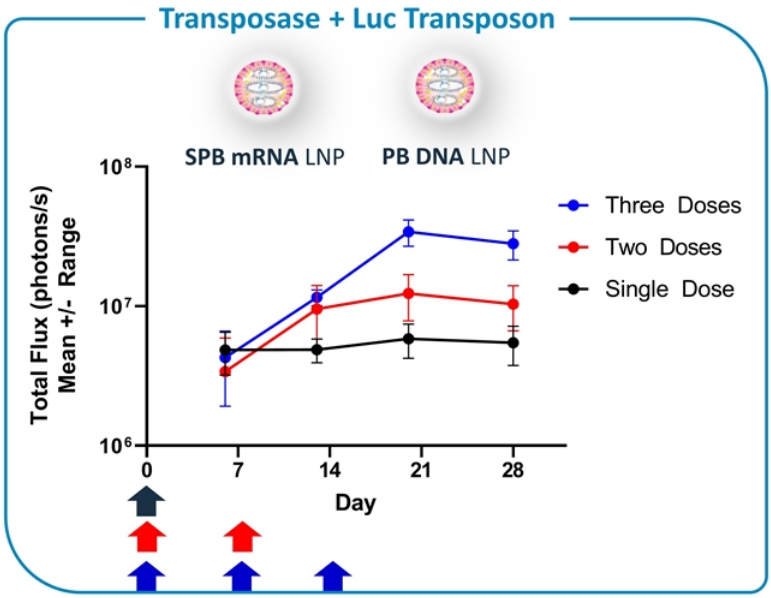
Representative Expression of Transposon DNA



- Representative efficacy for LNP formulated by Poseida with MC3 or other lipids.
- Mice administered 0.5 mg/kg of LNP comprising luciferase reporter transposon DNA

Nanoformulated PiggyBac® can be Dosed Repeatedly

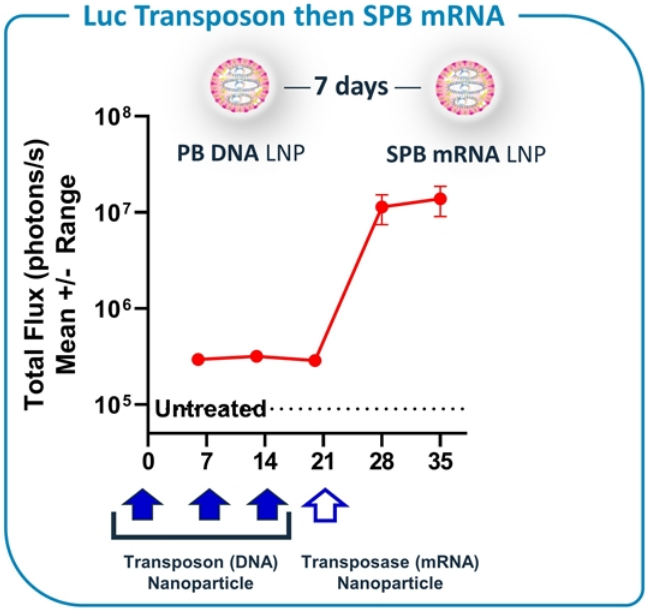
A Clear Advantage over AAV and Will Enable Clinical Optionality



- Adult wild type mice co-administered SPB mRNA and Transposon DNA LNP 1, 2, or 3 times at 7 day intervals
- Non-linear increase in transposon expression observed with each repeated dose
- Potential to titrate dose to obtain desired level of transgene expression

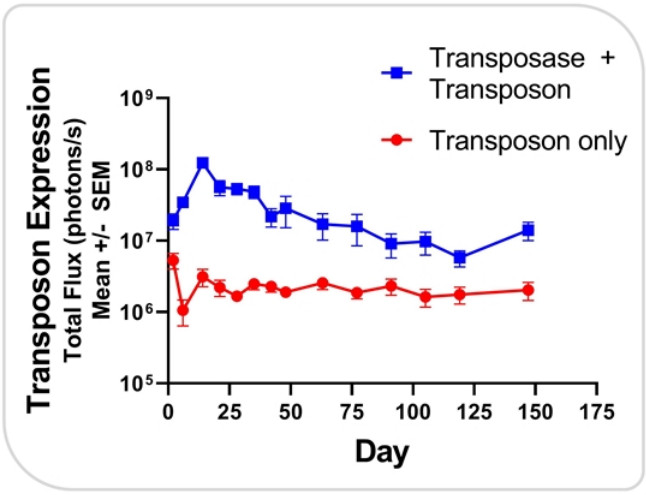
Transposon and Transposase can be Dosed Separately

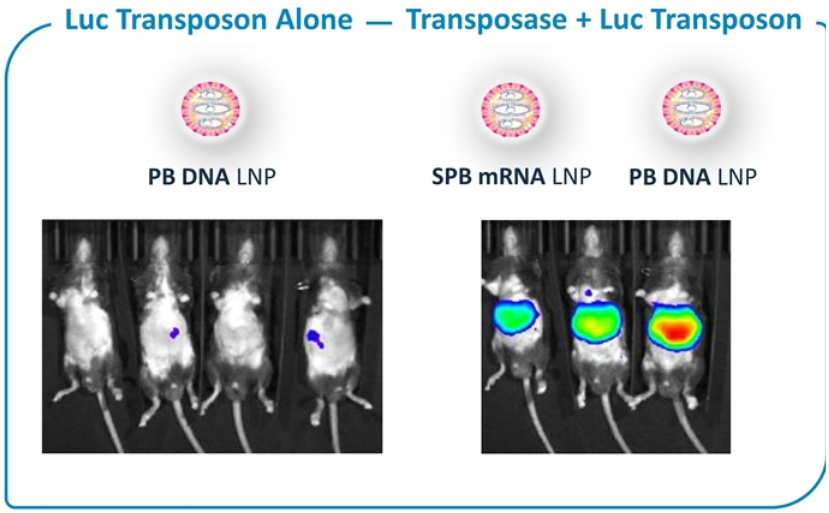
Potential to Optimize Dose Regimens by Indication If Needed



- Adult wild type mice administered Transposon DNA LNP alone 3 times at 7 day intervals, then administered a single dose of SPB mRNA LNP on day 21.
- SPB transposase and transposon dosing can be separated temporally
- Administration of SPB transposase (mRNA) can mobilize previously delivered transposon

Transposon and Transposase Co-Delivery Results in Sustained Transgene Expression in Juvenile Mice





Poseida Other Proprietary Tools

POSEIDA THERAPEUTICS

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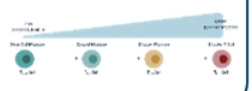


Proprietary and Highly Differentiated Technologies in a Competitive Cell and Gene Therapy Space

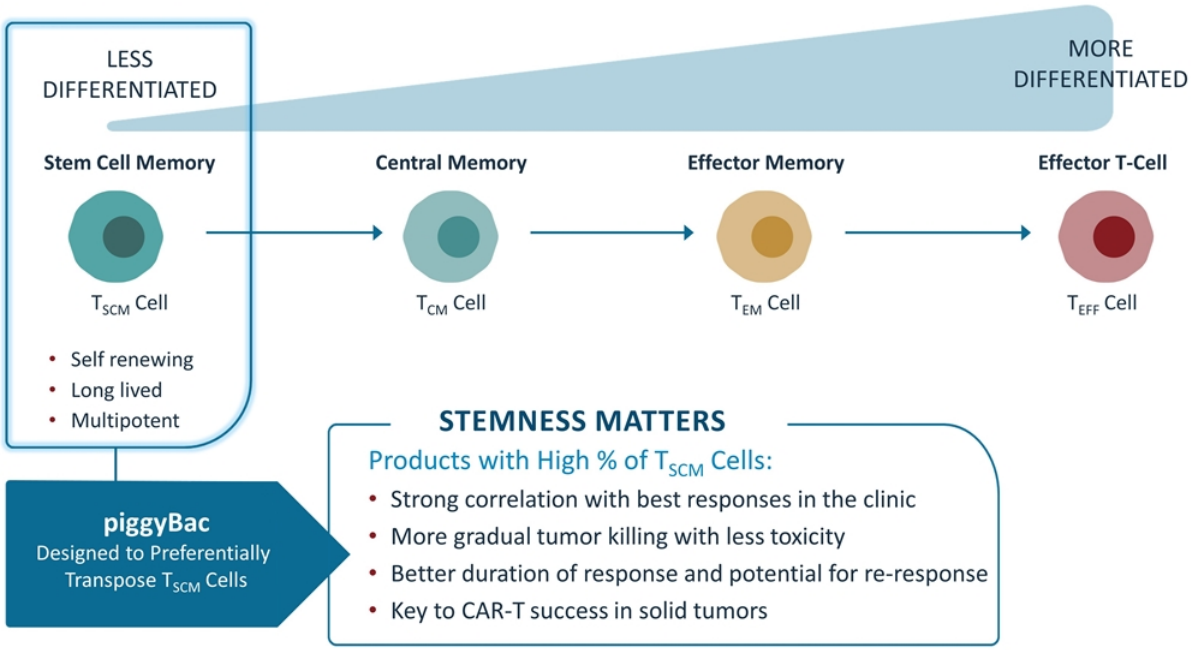
POSEIDA THERAPEUTICS

T_{scm} Manufacturing

POSEIDA THERAPEUTICS

Not All T-Cells are Created Equally

The Importance of Stem Cell Memory T Cells (Tscm)



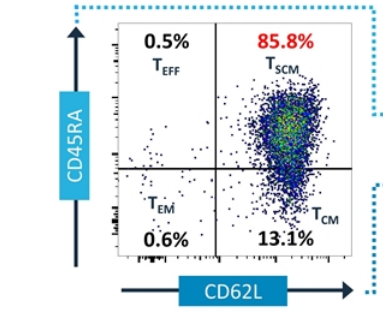
piggyBac
Designed to Preferentially Transpose T_{SCM} Cells

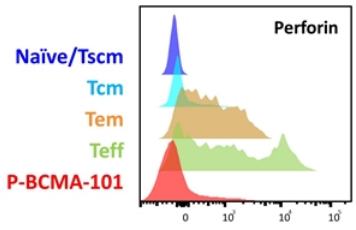
STEMNESS MATTERS

Products with High % of T_{SCM} Cells:

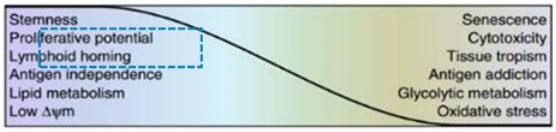
- Strong correlation with best responses in the clinic
- More gradual tumor killing with less toxicity
- Better duration of response and potential for re-response
- Key to CAR-T success in solid tumors

Stem Cell Memory T_{SCM} Phenotype





	T_N	T_{SCM}	T_{CM}	T_{EM}	T_{TE}	P-BCMA-101
CD45RA	+	+	-	-	+	+
CD45RO	-	-	+	+	-	-
CCR7	+	+	+	-	-	+
CD62L	+	+	+	-	-	+
CD28	+	+	+	+/-	-	+
CD27	+	+	+	+/-	-	+
IL-7Rα	+	+	+	+/-	-	+
CXCR3	-	+	+	-	-	+
CD95	-	+	+	+	+	+
CD11a	-	+	+	+	+	+
IL-2Rβ	-	+	+	+	+	+
CD58	-	+	+	+	+	+
CD57	-	-	-	+/-	+	-



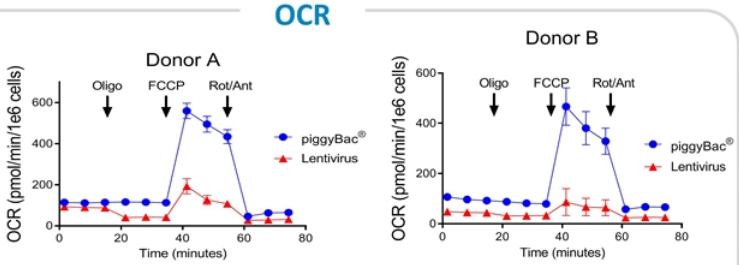
Adapted from Gattinoni et al. (2017) Nat. Med.

Our product more closely matches a T_{scm} phenotype when we do extensive cell surface markers and even intracellular markers

POSEIDA THERAPEUTICS

Poseida CAR-T Cells Exhibit Greater Mitochondrial Respiratory Capacity Compared to a CAR-Ts Generated by a Lentivirus Process

OCR

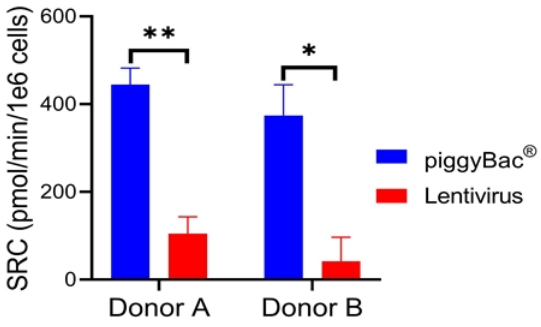


OCR: Oxygen consumption rate

Oligo: Oligomycin is an ATP synthase inhibitor,
FCCP is a protonophore that uncouples ATP synthesis from oxygen consumption
Rot/Ant: Rotenone is a Complex I inhibitor and antimycin A is a Complex III inhibitor

- **The greater metabolic reserves (respiratory capacity) of Poseida CAR-T cells may confer greater durability**

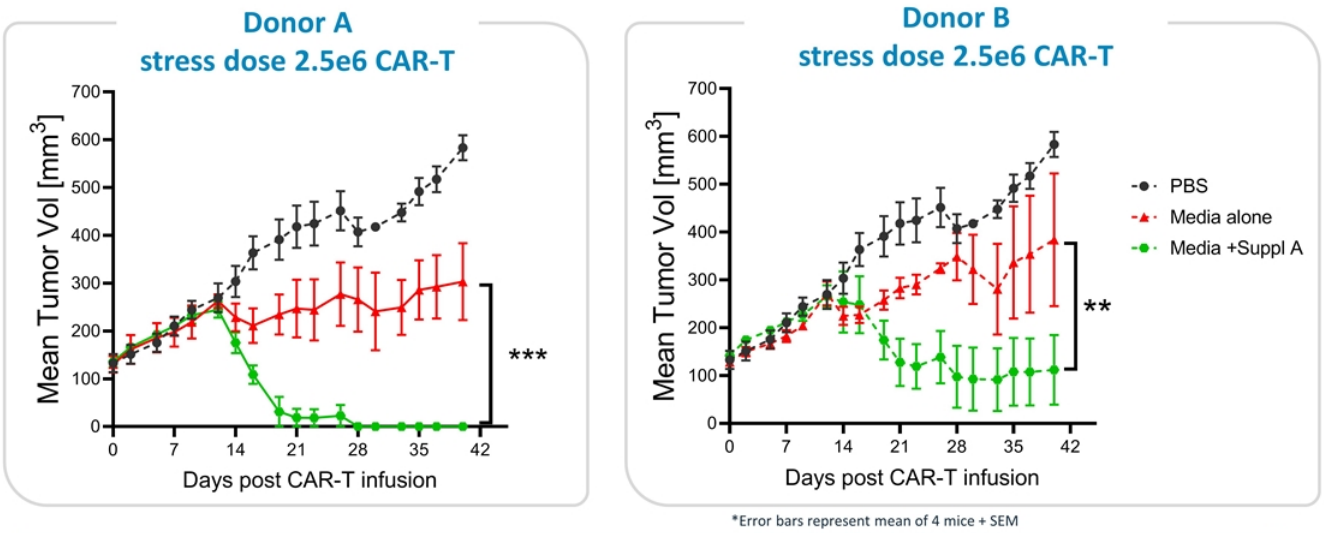
SRC



SRC: Spare Respiratory capacity

POSEIDA THERAPEUTICS

Addition of Supplement A Improved Product Performance In Vivo



*Error bars represent mean of 4 mice + SEM

Media + Suppl. A significantly improved final product function at the “stress” dose in a breast cancer model

Booster Molecule

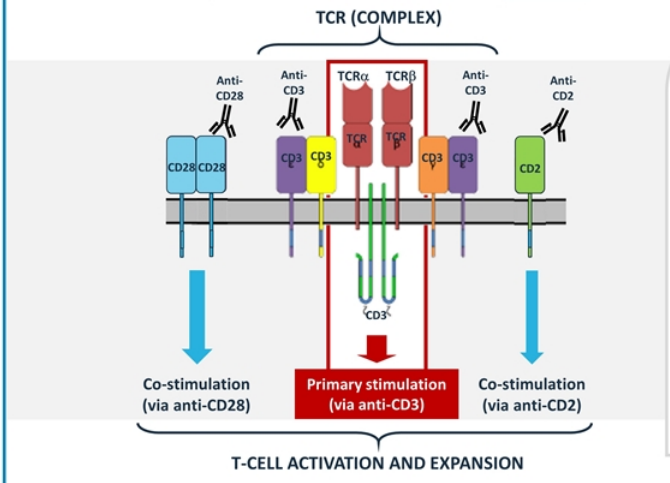
POSEIDA THERAPEUTICS

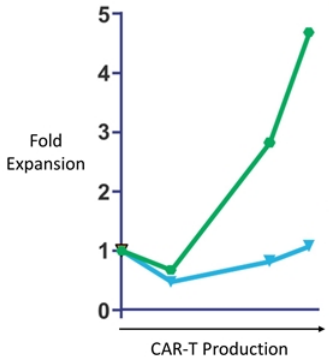
Our Booster Molecule Technology – Potential to Overcome the "Allo Tax" Common to Other Allogeneic CAR-T Approaches

THE PROBLEM:

Gene Editing of TCR Can Impair Allogeneic CAR-T Manufacturing

Compared to Unedited CAR-T = "Allo Tax"





With Booster

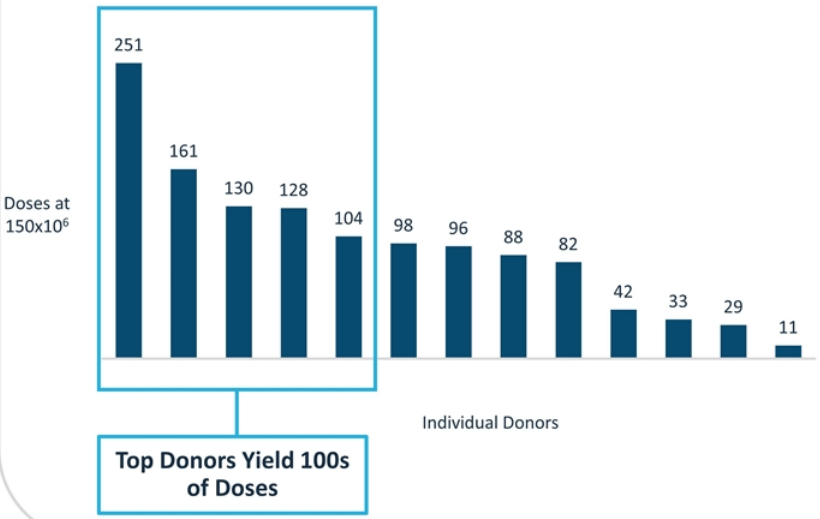
Our patented technology is designed to overcome these limitations, and **significantly increase production yield** while **preserving desirable T_{SCM} attributes** of P-BCMA-ALLO1

Without Booster

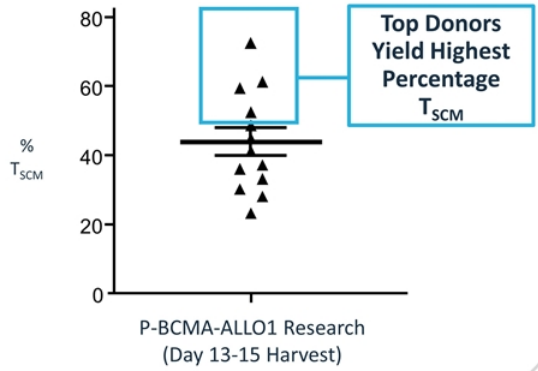
POSEIDA THERAPEUTICS

P-BCMA-ALLO1: Our Booster Molecule Technology in Action

Increase Fold Expansion of CAR-T



Preserve High % of T_{SCM} Cells



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Armoring Platforms

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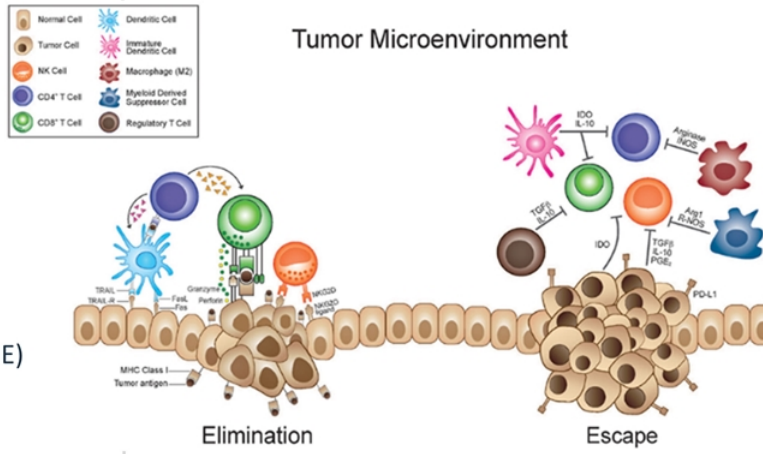
“Armoring” – Do We Need It?

Conventional Experience and Perception

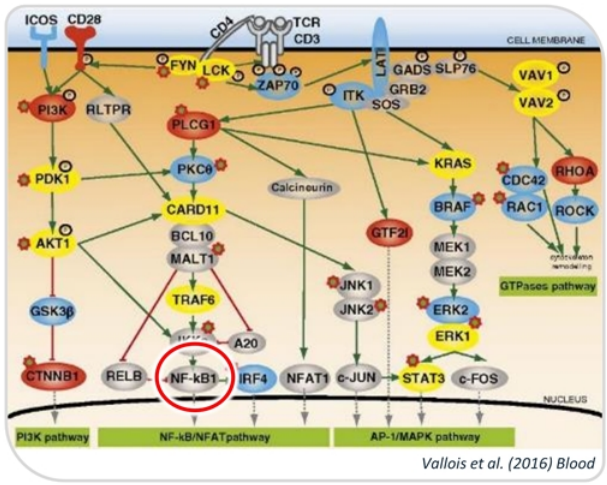
- Blood (liquid) tumors are easier to access by infused CAR-T cells
- Poor CAR-T responses in solid tumors to date
  - Only rare instances of Complete Responses (GBM, HCC) have occurred and only **after multiple CAR-T administrations**
- Solid tumor hurdles:
  - Tumor architecture, antigenic heterogeneity
  - Immunosuppressive tumor microenvironment (TME)
    - PD-L1, TGFβ, IL6, IL10, etc…
    - Tregs, MDSC, TAM, etc…
    - Glycolytic desert, low O2, pH, etc…



Monjazeb et al. (2013) Frontiers Oncol

Conditional Gene Expression System (GES)

- Can we exapt the TCR signaling pathway to express genes only upon CAR binding?
  - Inducible expression of a gene upon CAR-T binding
    - secretion of checkpoint inhibitor or cytokine
  - Turn a specific gene on or off
    - Cas9 to create indel or dCas9 plus repressor or activator
  - Change regulation of a gene
    - dCas9 plus methylase, deacetylase, etc…
- Which could then be used for:
  - **Armoring** – enabling enhanced CAR-T function in certain tumor environments
  - **Indicator cells** – using the T cell (or equivalent cell line) as an indicator of something (e.g., tonic signaling)
  - **Synthetic biology 101**
    - A CAR can probably be designed to bind just about anything (even specific nucleic acids)
    - The T cell is a "bag of killing enzymes", but could eventually be engineered to do much more



Vallois et al. (2016) Blood

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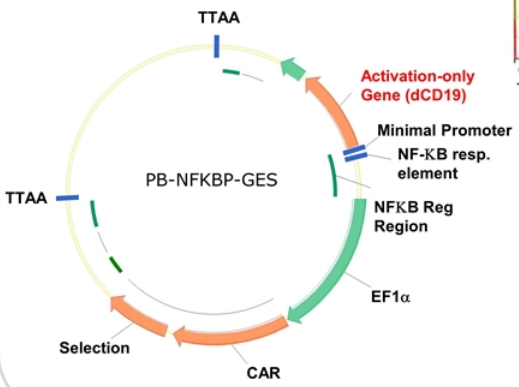
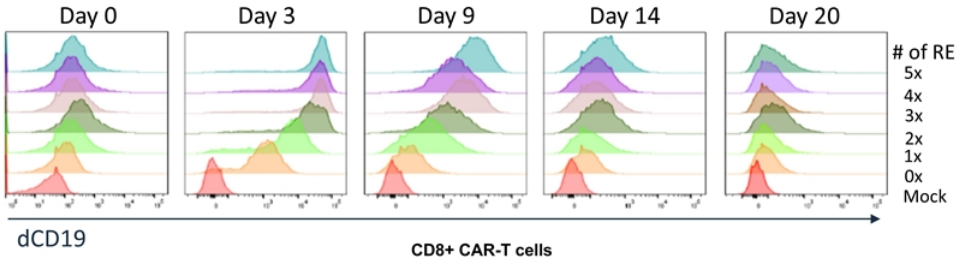
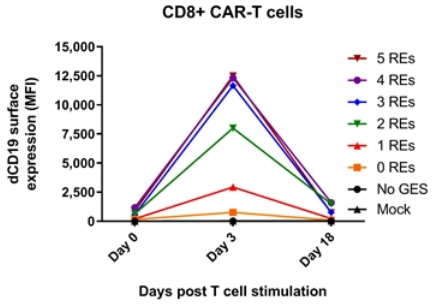
Conditional Gene Systems - Armoring

Enabling enhanced CAR-T function in certain tumor environments:

- For localized expression of Supporting cytokines, Pro/anti-inflammatory mols, Checkpoint blockade reagents, etc…
- Not leaky







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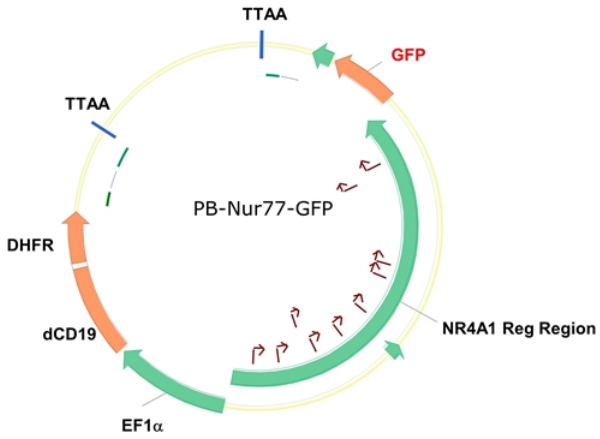
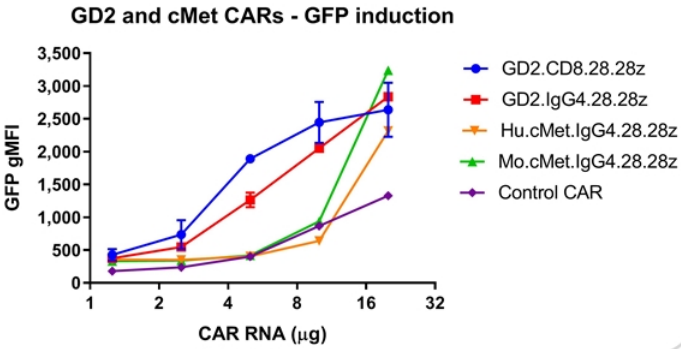
Conditional Gene Systems – Indicator Cells

Indicator Cells - For indicating tonic signaling



Long et al. (2015) Nat. Med.

Frigault et al. (2015) Can. Immunol. Res.



Poseida Therapeutics: Investment Hypothesis

Multiple Avenues to Significant Value Creation

Compelling Investment Hypothesis

- **Innovative and disruptive technology platforms** enable broad **cell and gene therapy** pipeline
- Multiple differentiated **autologous and allogeneic CAR-T** programs
- Novel **Gene Therapy** programs address shortcomings of AAV and enabling single treatment cures
- Significant opportunities for **partnership, collaboration and platform expansion** beyond current pipeline
- Experienced and **proven management team**
- Supported by **premier investors** with a strategic focus

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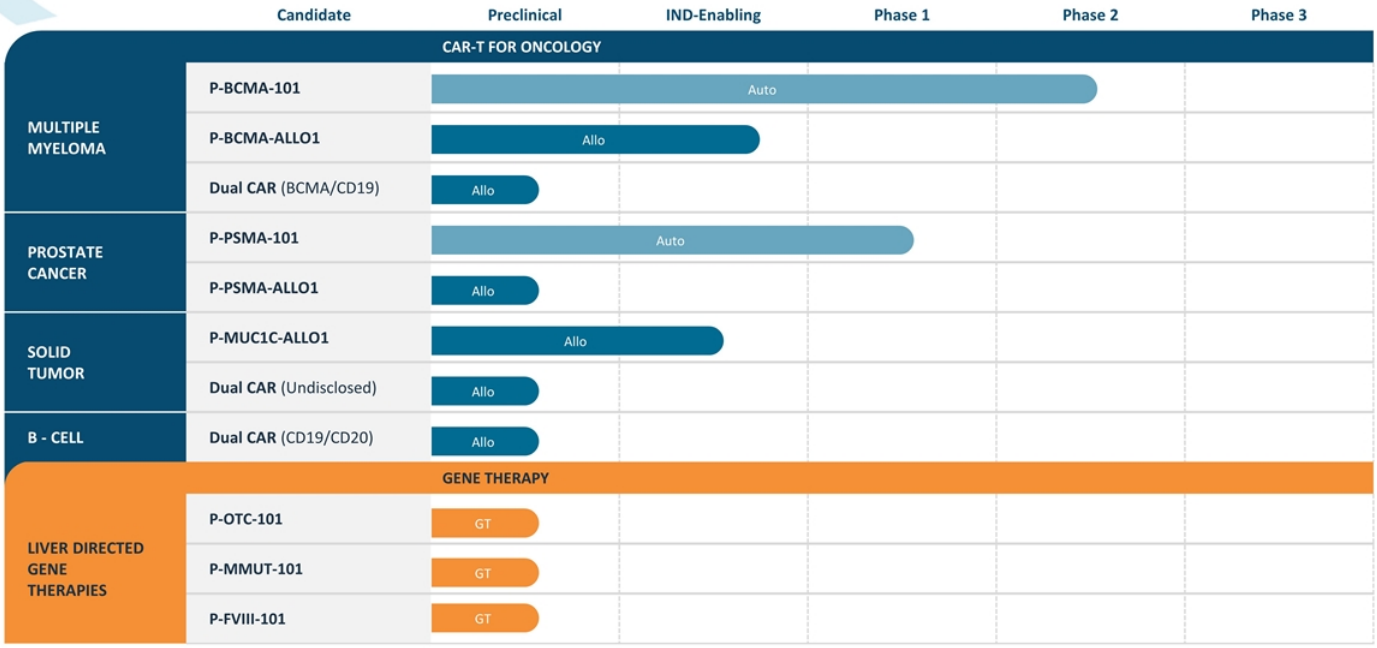
Current Cell and Gene Therapy Pipeline

All Programs Are Wholly-owned by Poseida



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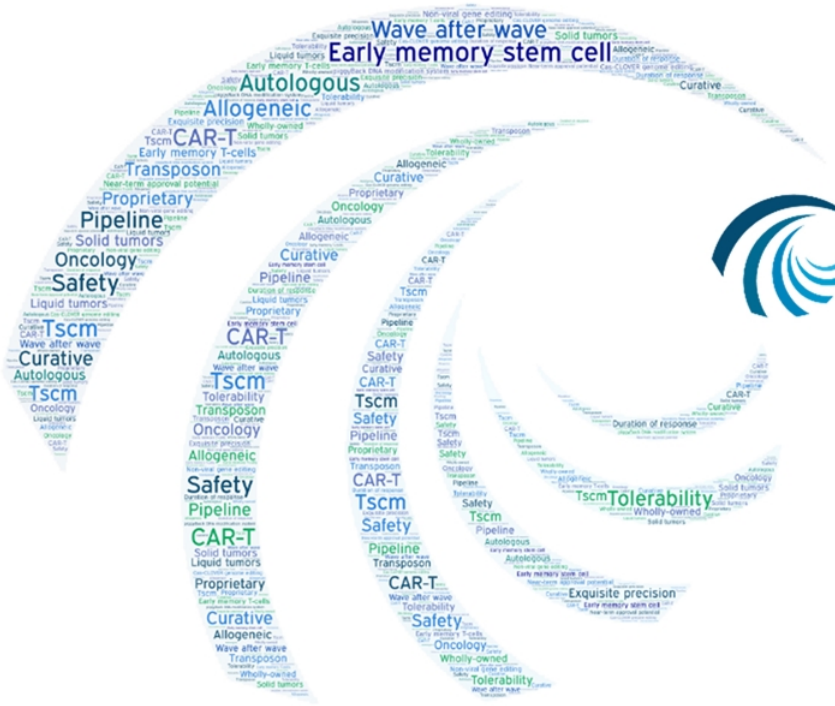

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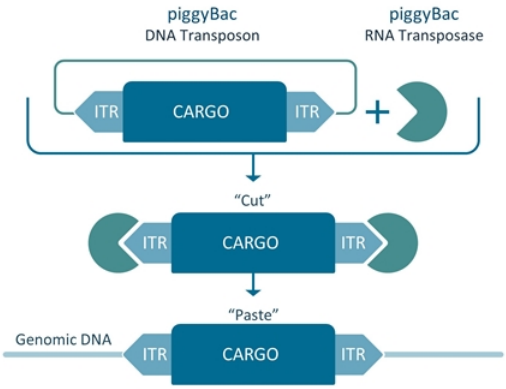
The Next Generation of Cell and Gene Therapeutics with the Capacity to Cure

Matthew A. Spear, M.D.
Chief Medical Officer

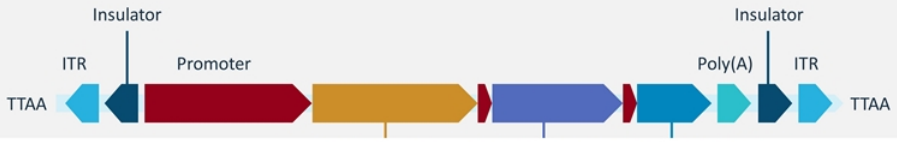
P-BCMA-101 & P-PSMA-101 are Novel Autologous CAR-T Cells Made With the piggyBac® Gene Delivery System

Very Large Cargo Capacity:
Potentially >20x Lentivirus



Large transgene with ability to carry multiple CAR or TCR molecule genes and armoring technology

Designed To Have Desirable Product Attributes



INCORPORATES PROPRIETARY SAFETY SWITCH

- Rapid, dose-dependent **elimination** of CAR-T cells with rimiducid if needed
- Potential **management of** Cytokine Release Syndrome (**CRS**) or other AEs

DIFFERENTIATED BINDING CAR-T MOLECULE

- Centyrin™ molecule with **high-specificity binding** to BCMA or PSMA
- Fully human with no **tonic signaling observed to date**

DRUG RESISTANCE GENE PERMITS POSITIVE SELECTION

- **~100% of T-cells** in final product express the CAR molecule
- Predicted to result in **greater therapeutic index**

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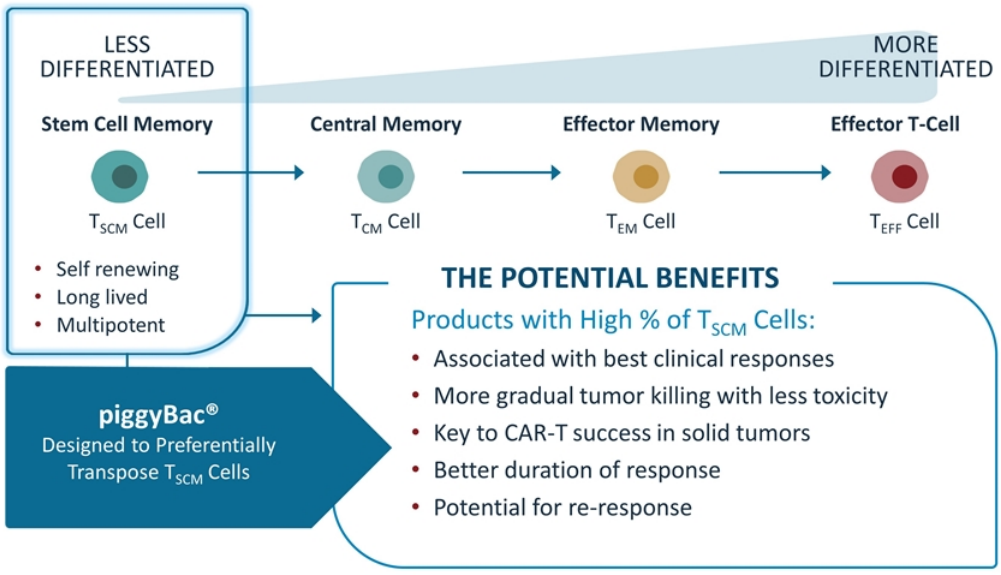
Not All T-Cells are Created Equally:
The Importance of Stem Cell Memory T Cells (T_{SCM})



Spear M., et al., Poseida (2019) CAR-TCR Summit; Melenhorst J. et al., UPenn (2017) 20th ASGCT; Basu et al., Adaptimmune (2017) CAR-TCR Summit; Bot A., et al., Kite (2019) CAR-TCR Summit; T_{cm}: Larson, Juno(2018) AACR; T_{scm} TIL: Beatty M., Moffitt (2018) SITC; T_{cm}: Fraietta J. et al., UPenn (2018) TET2 Disruption, PMID 29849141

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P-BCMA-101

POSEIDA THERAPEUTICS

P-BCMA-101: BCMA Targeted CAR-T Cells for Multiple Myeloma

MULTIPLE MYELOMA

- **~100K** patients in U.S.
- **~30K** new U.S. cases per year
- **~13,000** U.S. patient deaths / year

PROVEN TARGET

- **BCMA** expressed on essentially all MM cells
- **BCMA** specific to plasma cells and not on other normal tissues
- **Important** for tumor growth so antigen escape unlikely

NEAR-TERM STATUS

- ✓ **Phase 1/2 Clinical Trial Ongoing**
- ✓ **1st patient 2017**
- ✓ **Phase 2 initiated 2019**
- ✓ **Exploratory Phase 1 initiated 2020**
- ✓ **Awarded RMAT & orphan status**

[1]*http://ir.celgene.com/releasedetail.cfm?releaseid=1055252*

**Phase 3 may not be necessary if Phase 2 can serve as a registrational clinical trial. The FDA has indicated that if data from our planned Phase 2 clinical trial do not provide evidence sufficient for accelerated approval, additional clinical testing would be required, including potentially a randomized controlled trial or trials*

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P-BCMA-101-001 Phase 1/2 r/r Multiple Myeloma Clinical Trial

Phase 1 Trial Design

- Open Label, 3+3 Design, Single Ascending Dose Study
- 30 mg/m2 & exploratory cohorts
    - Allowance for **2nd dose** and retreatment **after other CAR-Ts**
  - **Cyclic dosing** exploratory cohorts
  - **Rituxan** and **Revlimid** exploratory cohorts
  - **Outpatient** administration allowed
- Up to 120 subjects

Phase 2 Trial Design (initiated but awaiting final dose selection)

- Same schema as Phase 1
- 112 subjects

Initial dose escalation completed

Expansion ongoing to test modified manufacturing process and novel dosing regimens

Clinical Trial Sites

Colorado Blood Cancer Institute- Tara Gregory, M.D.
Hackensack University Medical Center- David Siegel, M.D.

Johns Hopkins- Syed Abbas Ali, M.D.
Karmanos Cancer Institute- Abhinav Deol, M.D.

MD Anderson Cancer Center- Krina Patel, M.D.
Swedish Cancer Institute- William Bensinger, M.D.

Tennessee Oncology- Jesus G. Berdeja, M.D.

UC San Diego Moores Cancer Center- Caitlin Costello, M.D.
UC San Francisco- Nina Shah, M.D.
UC Davis- Mehrdad Abedi, M.D.

University of Chicago- Andrzej Jakubowiak, M.D.

University of Kansas Cancer Center- Siddhartha Ganguly, M.D.

University of Maryland- Mehmet Kocoglu, M.D.

University of Pennsylvania- Adam Cohen, M.D.

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RMAT

Modified Manufacturing Process Using Nanoplasmids (NP)

Small Changes in CAR-T Manufacturing Can Have a Big Impact

- Cell-based products are **living drugs** and are affected by donor and manufacturing variability. The **type and quality of cells** affect product performance
- Improving **transposition frequency** during manufacturing may improve final product
  - More CAR+ cells, less cell proliferation and cell death in culture means healthier more proliferative cells in a patient
- Improving Transposition of P-BCMA-101 with a Modified Manufacturing Process with **Nanoplasmid (NP)**
- Incorporated manufacturing changes that increases transposition frequency 2X on average

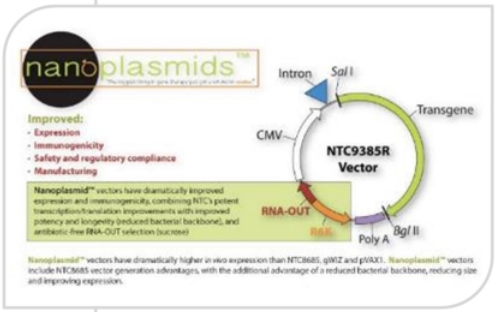
Improving Transposition of P-BCMA-101 with a Modified Manufacturing Process with Nanoplasmid (NP)

Standard Plasmid

- Antibiotic resistance marker and replication origin (> 2,000 bp)

Nanoplasmid (NP)

- Reduces the backbone size to < 500 bp (less DNA = less toxicity)
- Brings piggyBac® ITRs closer together (enhanced transposition efficiency)
- Antibiotic-free selection (superior for manufacturing and regulatory)
- Higher manufacturing yield
- Safety demonstrated in multiple clinical trials



* Nanoplasmid is a trademark of Nature Technology Corporation (NTC) and nanoplasmids are licensed from NTC

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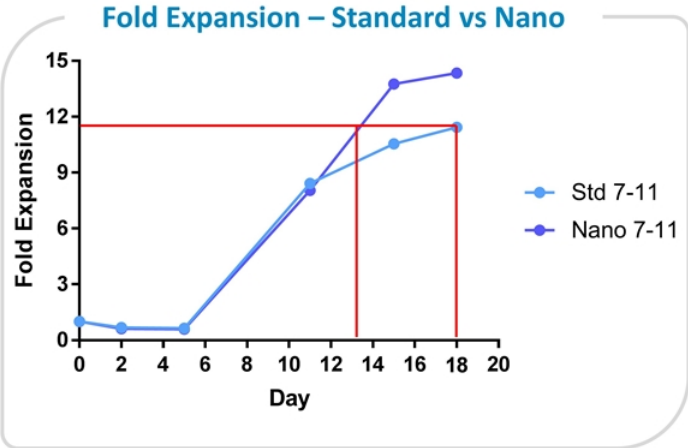
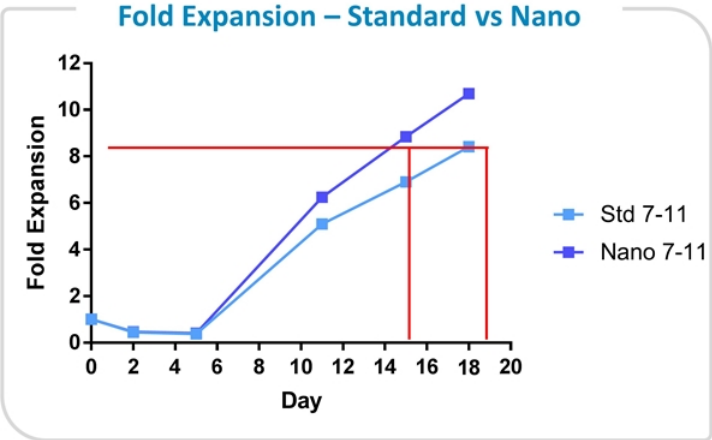
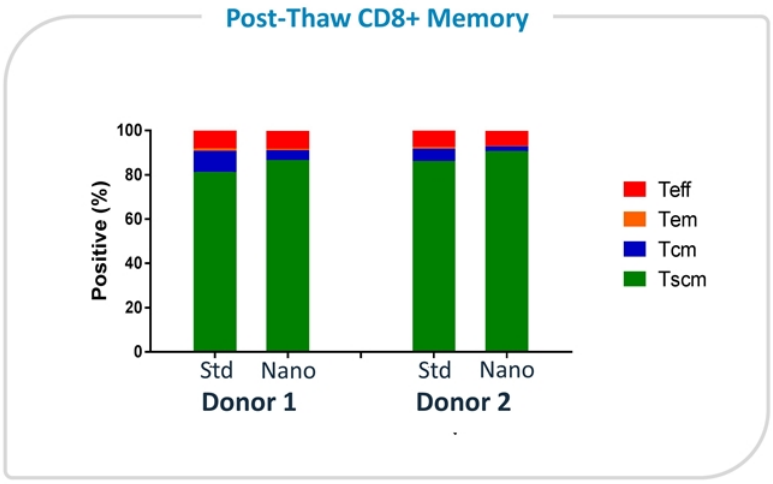
Nanoplasmid Shortens Manufacturing Time





CAR-T product made from nanoplasmid reaches the same number of cells as CAR-T made from standard plasmid in ~4 fewer days

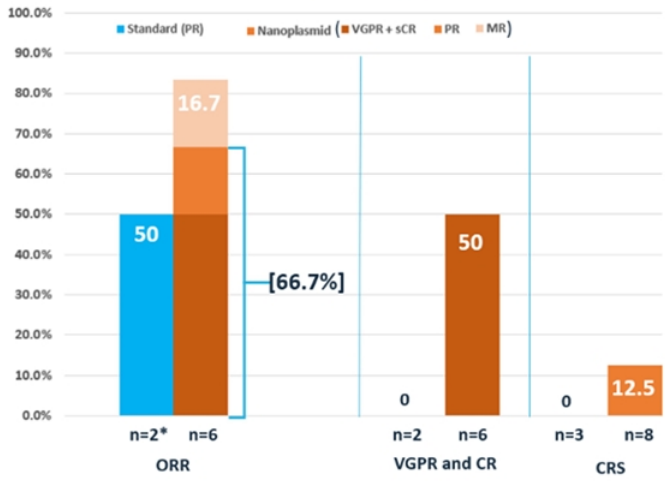
Nanoplasmid-produced CAR-T Show Increased %T_{SCM}



Initial Dose Escalation with Nanoplasmid (NP) Manufacturing Process: Equal Safety and Better Response Compared to Standard Plasmid

- P-BCMA-101 **with Nanoplasmid demonstrated higher ORR** than P-BCMA-101 with standard plasmid
  - 66.7% vs 50% by IMWG
- P-BCMA-101 **Nanoplasmid delivered deeper responses** than P-BCMA-101
  - 3 P-BCMA-101 Nanoplasmid patients at VGPR or CR compared to zero for standard plasmid
- **Safety profile** was preserved with **one Grade 1 CRS** observed with either product in these patients

Standard Plasmid vs. Nanoplasmid @ Cohort 1 Dose Level



ORR for cyclic dosing was 1/4 (PR), Cmax was low and followed individual administrations without expanding AUC
*3 patients dosed but only 2 evaluable by IMWG criteria. 3rd patient had plasmacytomas and had significant response by PET scan.
Data cutoff: November 16th, 2020. ORR Objective Response Rate, attaining sCR, CR, VGPR or PR, including confirmed and unconfirmed responses.
Evaluable patients: Obtained first response assessment by IMWG m-protein criteria or PD/death.

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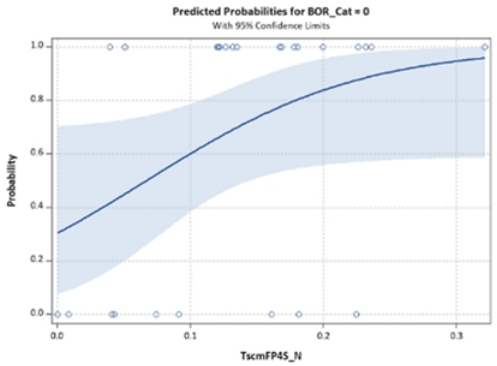
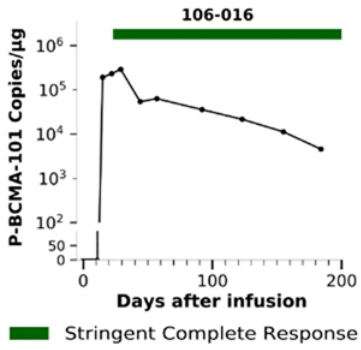
Data Demonstrate Efficacy, Durability and Safety of P-BCMA-101

Unparalleled Safety and Persistence

T_{SCM} Correlates with Best Responses



Can Persist In Vivo



And Offers A Superior Safety Profile

- 16 patients dosed **fully outpatient**
- All CRS was Grade 1/2
- No to **very low neurotoxicity**
- **No ICU admissions for CRS**
- **No patient death due to P-BCMA-101**

- T_{SCM} in P-BCMA-101 is directly **correlated with best responses in the clinic**
- **Long-term persistence of T_{SCM} cells** in some patients
- Potentially best-in-class safety profile allows for **fully outpatient dosing**

Data cutoff: November 16th, 2020.

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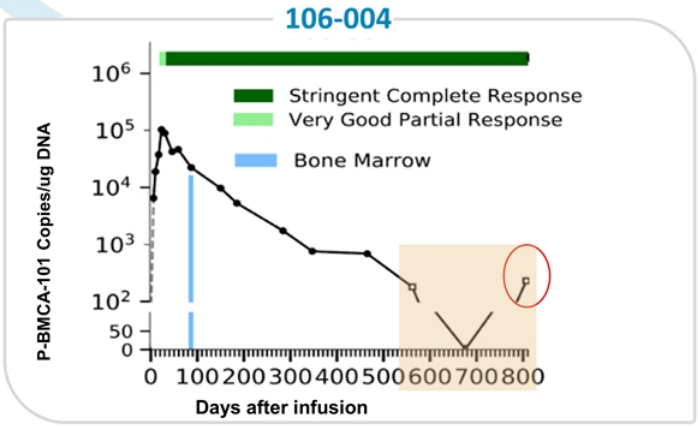
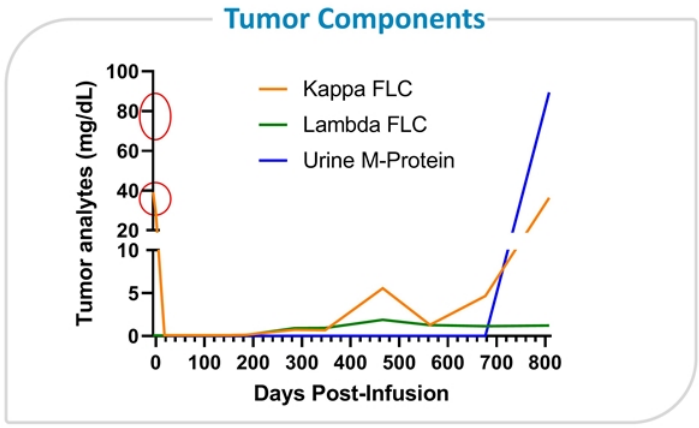
Case Study for P-BCMA-101 Persistence/Re-expansion: 106-004





- High Tscm
- Instance where a single dose led to long term persistence (~2yrs) and *re-expansion* of CAR-T
- Re-expansion in 106-004 coincides with an increase in MM tumor markers
- Out of 27 Bone Marrow samples tested, 106-004 has highest level of P-BCMA-101
- Demonstrates ability of T_{SCM} cells to home to bone marrow, engraft, create persistent CAR-T cells in the periphery, maintain stringent complete response for long duration and re-expand at tumor relapse

Summary

Safety & Efficacy with a Novel BCMA CAR-T Cell Product

- **Excellent safety and efficacy profile demonstrated in a standard dose escalation**
  - **Fully outpatient dosing enabled** with very low rates of CRS (17%, no Grade 3+), very low to no neurotoxicity, no ICU admissions
    - May allow for greater patient access (e.g., administration at community hospitals and/or outpatient sites)
  - **High percentage of stem cell memory T cell phenotype (T_{SCM})** may result in greater safety and efficacy, is correlated with best responses and may allow product to re-respond to tumor during relapse in some instances
- **Use of modified manufacturing process (Nanoplasmid) may improve expansion and efficacy**
  - Nanoplasmid increases transposition frequency, thereby shortening manufacturing time, and increases the percent of T_{SCM} cells, proliferative capacity and efficacy of the final product
  - Current process at 0.75X10e6 cells/kg dose results in 67% ORR, 50% VGPR/sCR with 12.5% CRS
  - Dose escalation is continuing in Nanoplasmid groups

P-PSMA-101

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P-PSMA-101: PSMA Targeted CAR-T Cells for Metastatic Castrate-Resistant Prostrate Cancer (mCRPC)

POPULATION

- **~2.8M** prostate cancer patients in US
- **~40K** new cases of mCRPC in US per year
- **27.5K** US patient deaths per year

PROVEN TARGET

- **PSMA** expressed on essentially most prostate cancer cells
- **PSMA** targeted successfully with ADC and RIT

UNMET NEED

- **High unmet need** for advanced disease
- **~25%** 5-yr survival for mCRPC patients

[1]*https://globenewswire.com/news-release/2017/02/02/913304/0/en/Prostate-Cancer-Market-Study-2017-Market-Size-of-Prostate-Cancer-Drugs-to-7b-in-2016-from-2-5b-in-2011.html*
[2]*https://www.researchandmarkets.com/research/wxtf93/global_prostate*

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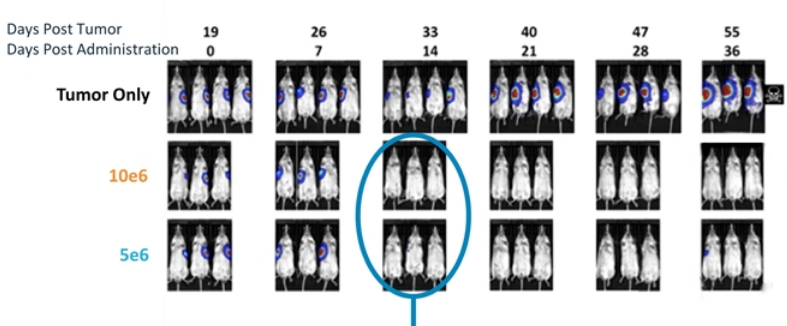
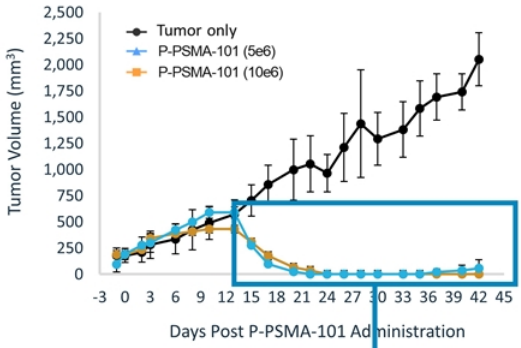
P-PSMA-101 Demonstrated Potent in vivo Activity

Efficacy of P-PSMA-101 in Prostate Cancer Model (LNCaP.luc)

Imaging



Caliper Measurement



Tumor Elimination in 100% of Animals at Standard and Low Doses After ~ 2 Weeks

Data presented at SITC 2017. One animal in the low dose cohort relapsed later in the study.

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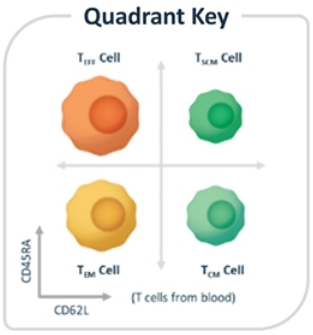
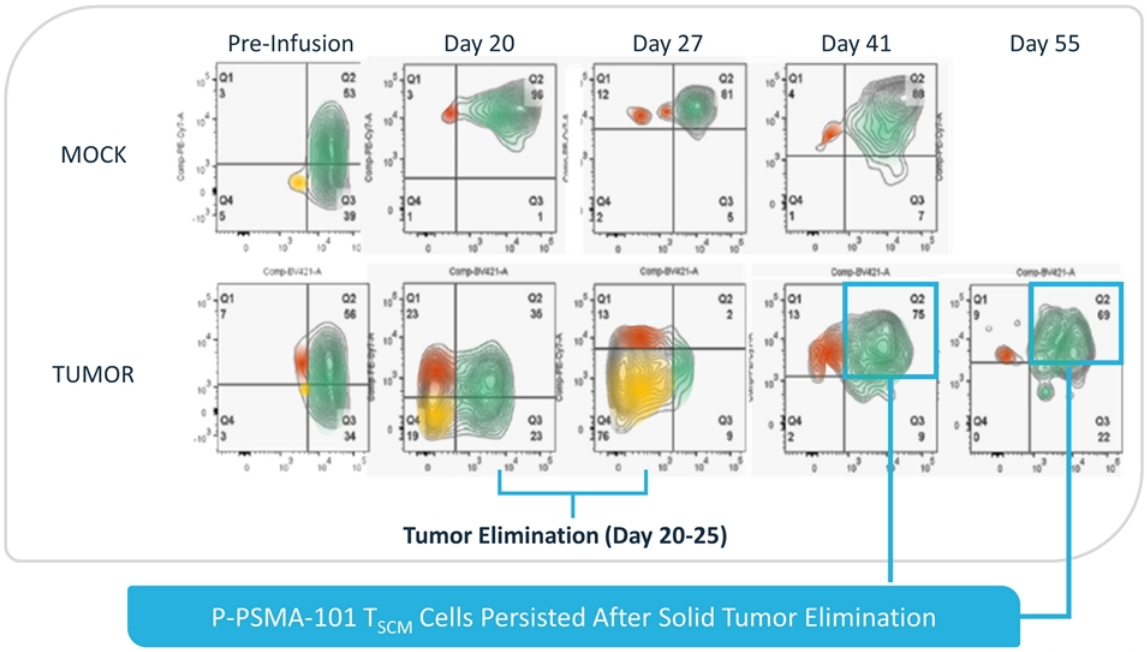
P-PSMA-101 Data Suggest Persistence of T_{SCM} Cells





Data presented at SITC 2017

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P-PSMA-101-001 Phase 1 Clinical Trial in mCRPC

Phase 1 Trial Design

- Open Label, 3+3 Dose Escalation
- 30 mg/m^2 fludarabine + 300 mg/m^2 cyclophosphamide x 3d lymphodepletion regimen
- P-PSMA-101 administered intravenously
  - Single dose and multiple dose cohorts (initiating with single)
  - Standard lymphodepletion and + Rituxan
- Up to 40 subjects

First Patient Treated in 2020

FDA Clinical Hold in August 2020

Apparent MAS, a known CAR-T effect
Responded with protocol amendment

Rapidly reopened trial in November 2020

Enrollment ongoing

Clinical Trial Sites

UC San Francisco- David Oh, M.D.

UC San Diego Moores Cancer Center- Rana McKay, M.D.

SCRI / St. Luke's- Gerald Falchook, M.D.

Dana-Farber- Xiao Wei, M.D.

Massachusetts General Hospital- Xin Gao, M.D.

City of Hope- Tanya Dorff, M.D.

Memorial Sloan Kettering- Susan Slovin, M.D.

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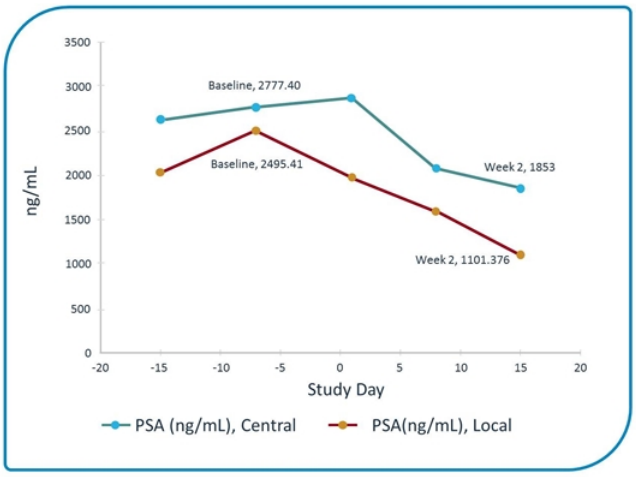
P-PSMA-101-001 Patient 17-206 Case Study

- **73 y/o male with mCRPC** after multiple lines of treatment, including biclutamide, Lupron, docetaxel, cabazitaxel, abiraterone, enzalutamide, crizotinib and anti-PSMA BiTE
- P-PSMA-101 administered on January 20th, 2021 (0.25 x 10e6 cells/kg; 20 x 10e6 total cells)
- Grade 1 CRS (fever, APR, LFT, cytokines) in the 2nd week, treated pharmacologically to resolution
- PSA rapidly decreased >50%



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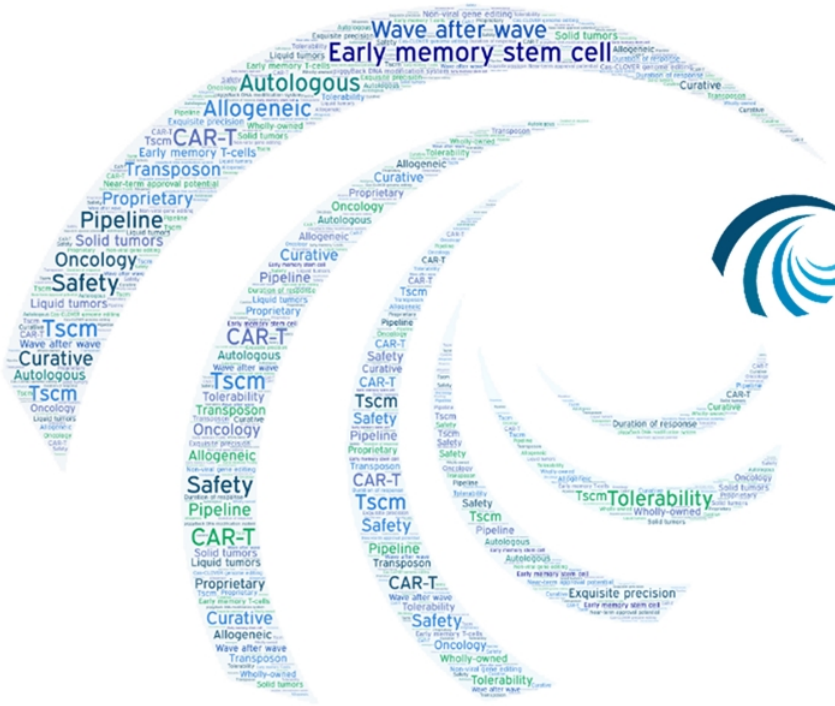
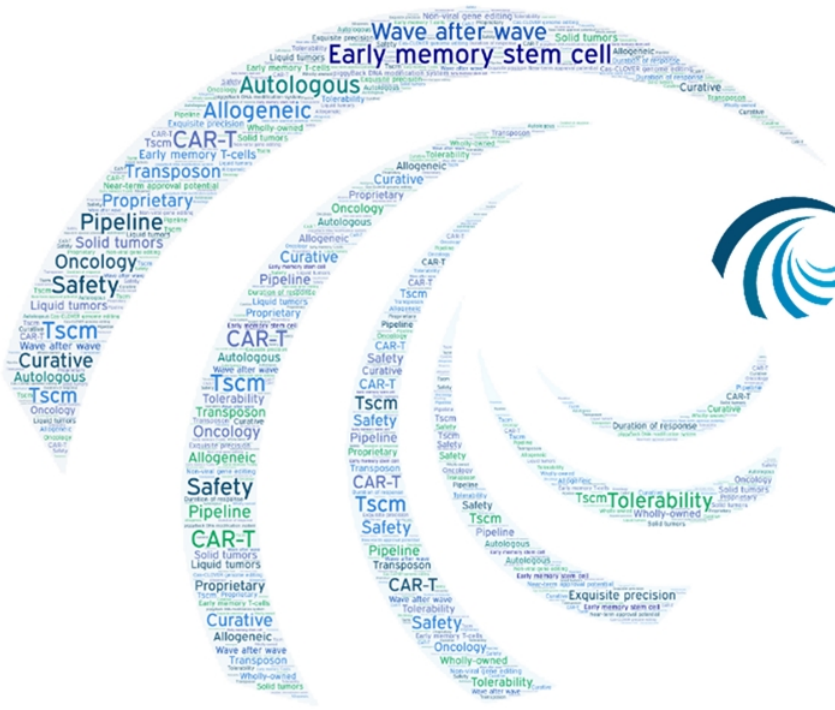
Summary

- Outstanding preclinical efficacy in mouse CRPC models
- Utilizing the same transposon design and NP manufacturing process as P-BCMA-101, thus similar benefits are expected
- Significant expansion of P-PSMA-101 cells in patients
- CRS can be seen but appears manageable when treated promptly
- One patient death and brief clinical hold after a significant patient non-compliance event where optimal pharmacologic intervention for CRS-spectrum toxicity was not possible
- Case study: P-PSMA-101 can elicit rapid and significant PSA declines >50%
- Dose escalation is ongoing and additional patient data will be reported later in year



POSEIDA THERAPEUTICS

The Next Generation of Cell and Gene Therapeutics with the Capacity to Cure



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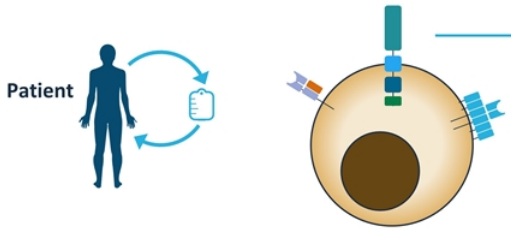
Cas-CLOVER™ Safety Profile: Examining Off-Target Activity

Blair Madison, Ph.D.
Senior Director, Genetic Engineering

Poseida Fully Allogeneic CAR-T Approach

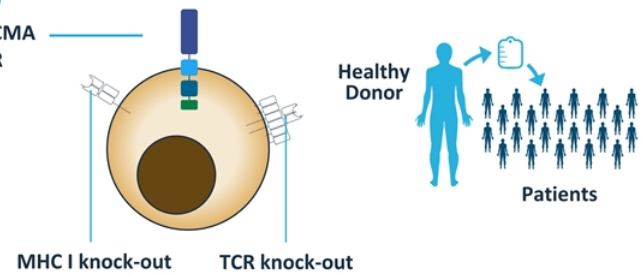
AUTOLOGOUS



CHALLENGES

- **Variable manufacturability** of patient material
- Long manufacturing **time**
- High **cost** of an individualized product

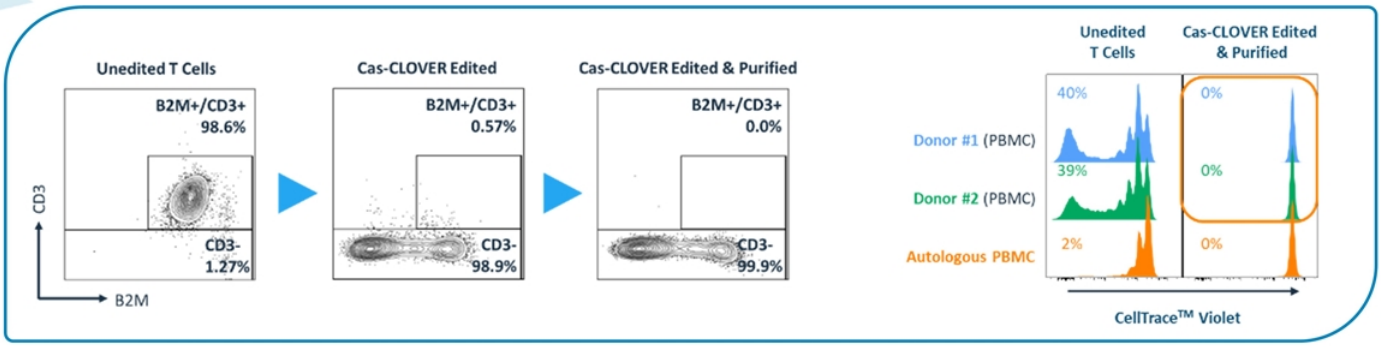
ALLOGENEIC



ADVANTAGES

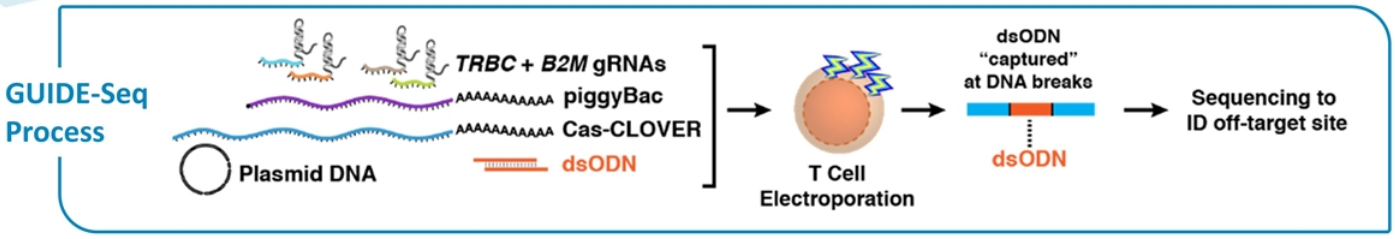
- **Quality:** Healthy donor material for consistent potency, higher %T_{scm} and ease of manufacturing
- **Universal:** Off-the shelf product for increased patient access
- **Scalability/cost:** Large number of doses for numerous patients from a single manufacturing run

Cas-CLOVER™ Efficiently Knocks-Out (KO) TCR in Resting T Cells

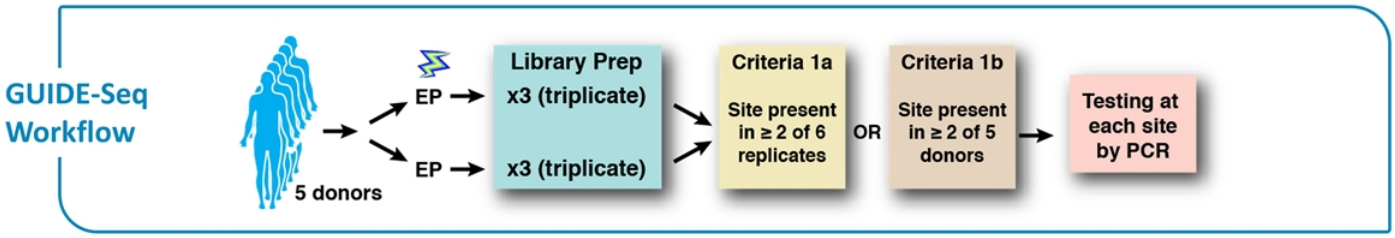


- For **off-the-shelf** allogeneic CAR-T products, **efficient TCR KO** is critical to **prevent graft versus host disease** (GvHD)
- Cas-CLOVER™ allows for **highly efficient TCR KO** across wide range of healthy donors with editing rates of up to 99%
- Residual TCR+ cells are removed resulting in a **highly pure TCR-negative CAR-T product** with up to 99.9% TCR KO
- Cas-CLOVER™ edited & purified cells do not exhibit alloreactivity/GvHD when mixed with donor-mismatched PBMCs

Off-Target Site Identification with GUIDE-Seq/Oligo Capture

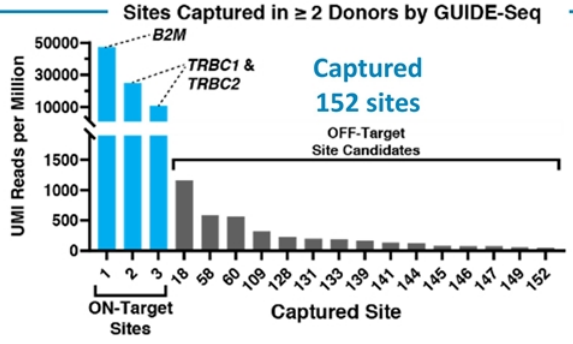


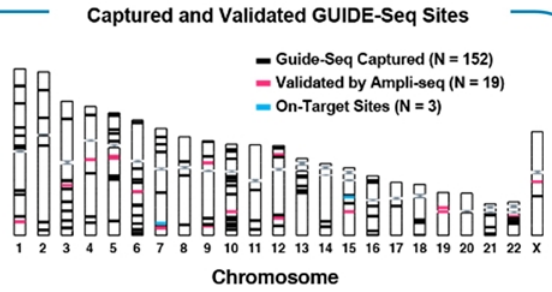
- *In cellulo* approach (capturing DNA breaks in real time)
- Unbiased, widely accepted, with high reproducibility
- Discovers candidate off-targets in context of manufacturing process



Off-Target Site Identification with GUIDE-Seq/Oligo Capture

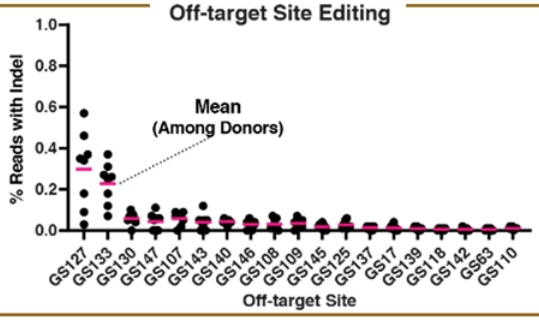
GUIDE-Seq





No hits in cancer-relevant genes

PCR & Amplicon-Seq



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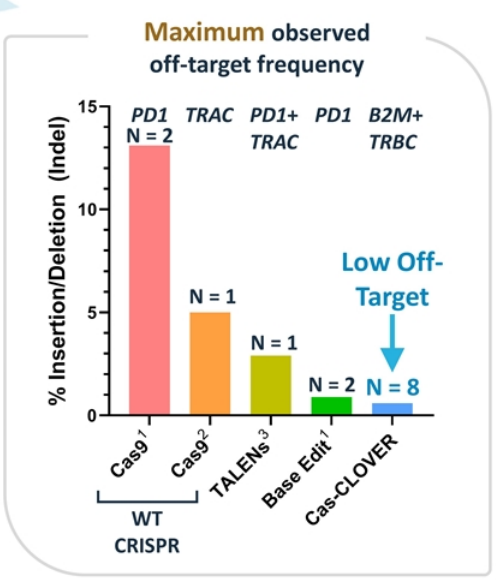
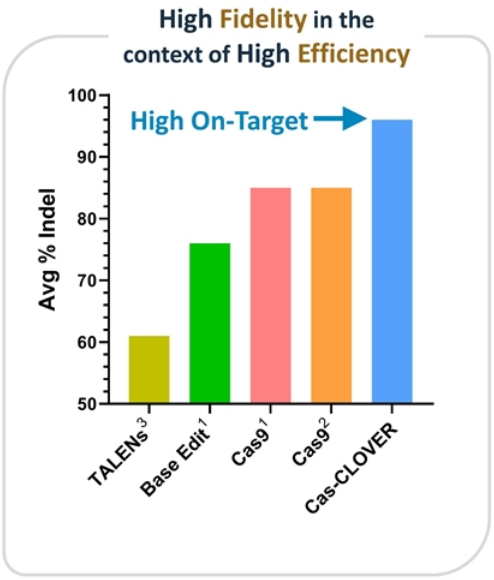
Cas-CLOVER Fidelity in T Cells vs. Competing Technology

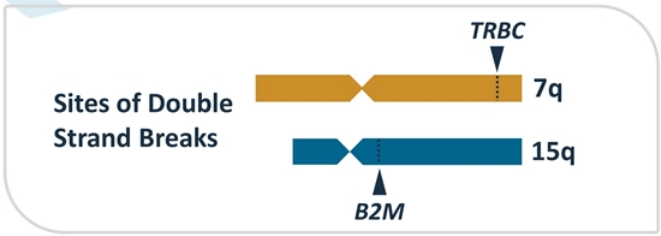


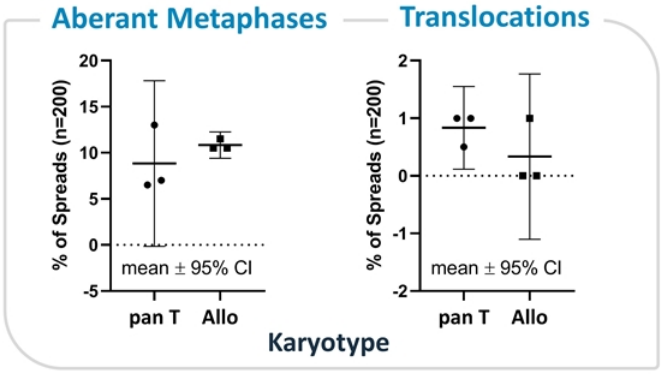
- Other studies examine few (10 to 25) candidate off-target sites[1-3].
- Our Cas-CLOVER off-target study is ~10x broader and includes 8 donor lots.

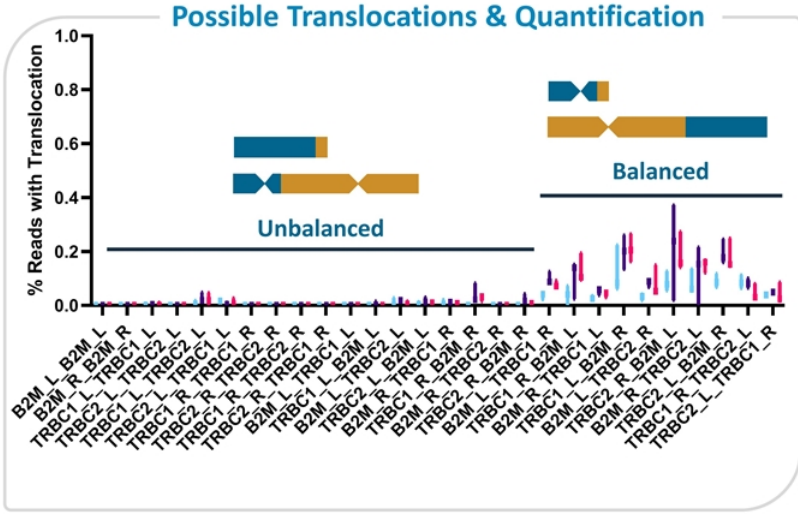


1. Webber et al., *Nat Commun.* 2019 Nov 19;10(1):5222.
2. Ren et al., *Oncotarget*. 2017 Mar 7; 8(10): 17002–17011.
3. Gautron et al., *Mol Ther Nucleic Acids*. 2017 Dec 15;9:312-321.

Cas-CLOVER™ Does Not Contribute to Genome Instability







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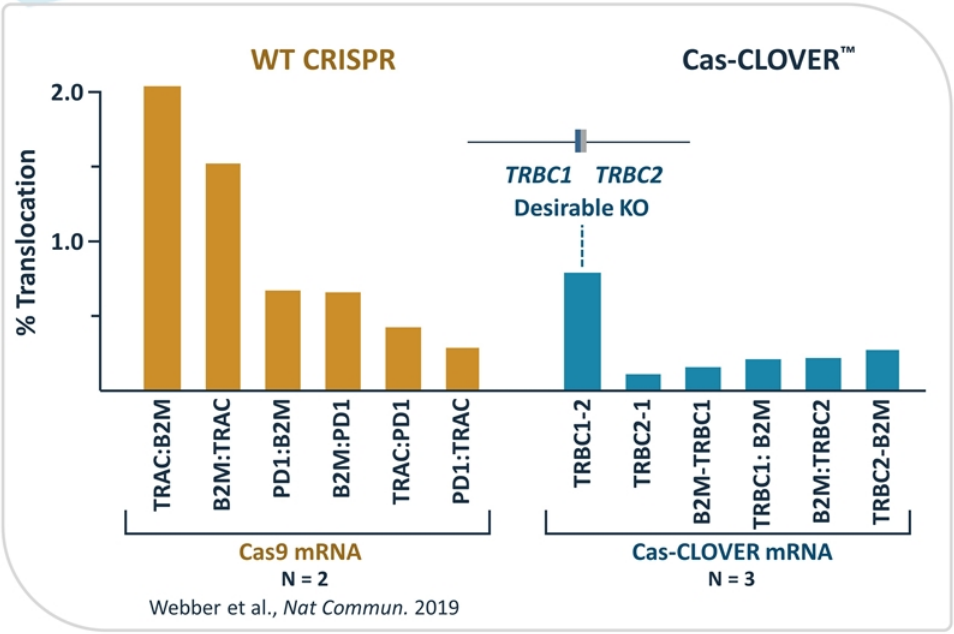
Translocations in T Cells: Cas-CLOVER™ vs. CRISPR



Webber et al., *Nat Commun.* 2019

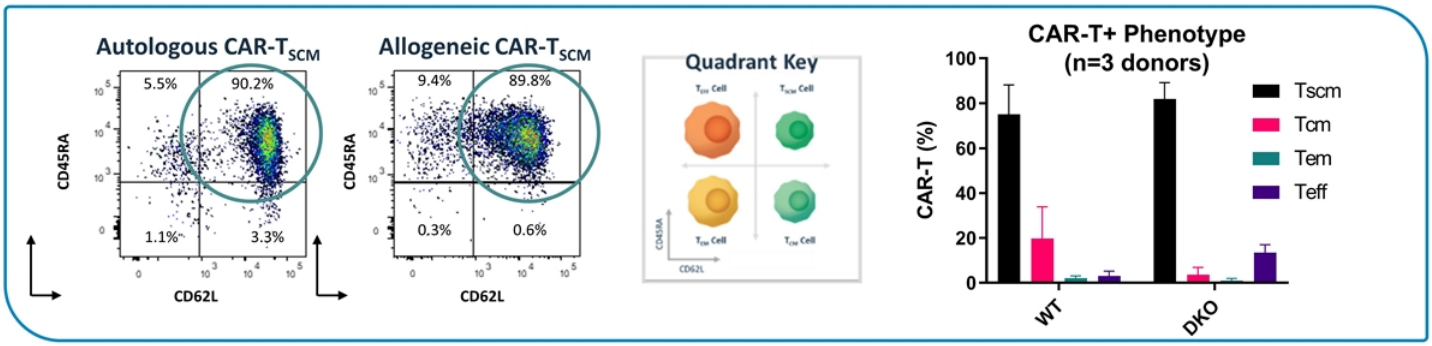
Cas-CLOVER™ Allogeneic CAR-T translocation rate <0.4%

Other studies (CRISPR & TALENs):

- **4% cells have *TRAC* translocation (FISH)**
  Qasim et al., *Sci Trans Med*. 2017
- **2-2.5% with *TRAC-B2M* translocation**
  Giannoukos et al., *BMC Genomics.* 2018
- **Up to 2% with *TRAC-CD52* translocations**
  Poirot et al., *Cancer Res*. 2015

With Cas-CLOVER™, the avg. rate of translocation with off-target sites <0.01%

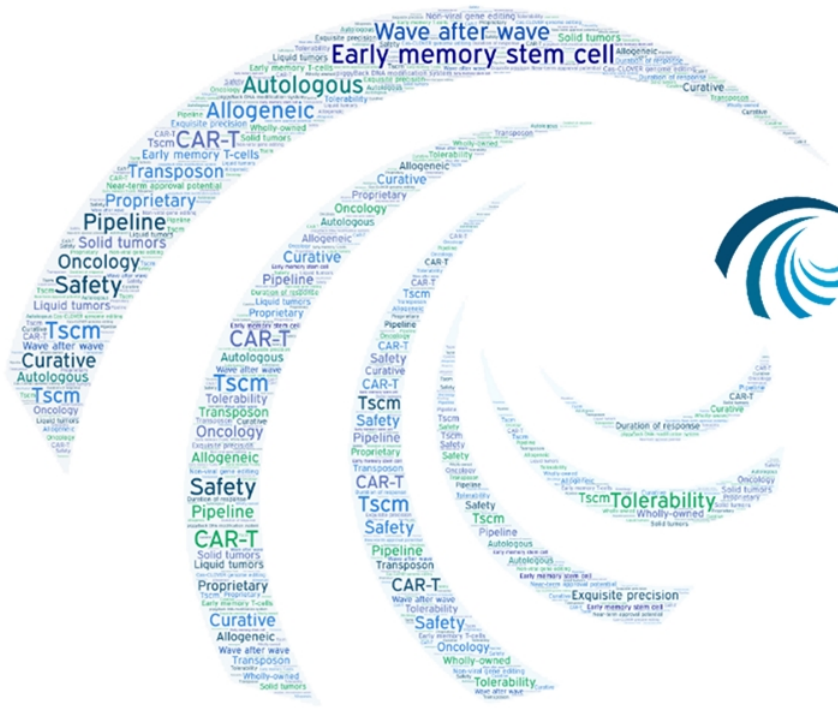
Cas-CLOVER™ Gene Editing in Resting T Cells for Generation of Fully Allogeneic CAR-T



- The **desirable T_{SCM} cell composition** is maintained in the finished allogeneic product
- A high T_{SCM} composition contributes to **a favorable tolerability profile, likely enabling fully outpatient dosing** similar to Poseida's autologous product candidate (P-BCMA-101)
- Other allogeneic CAR-T products report low % **T_{scm}** (1-9% in published reports)

Summary

- The Cas-CLOVER™ yields highly efficient multi-gene knockouts in resting T cells
- Cas-CLOVER™ exhibits no (or very low) unwanted off-target activity and is thus the “cleanest” site-specific genetic editing system in the industry
- Cas-CLOVER™ does not adversely affect large-scale genome stability
- Tscm composition maintained



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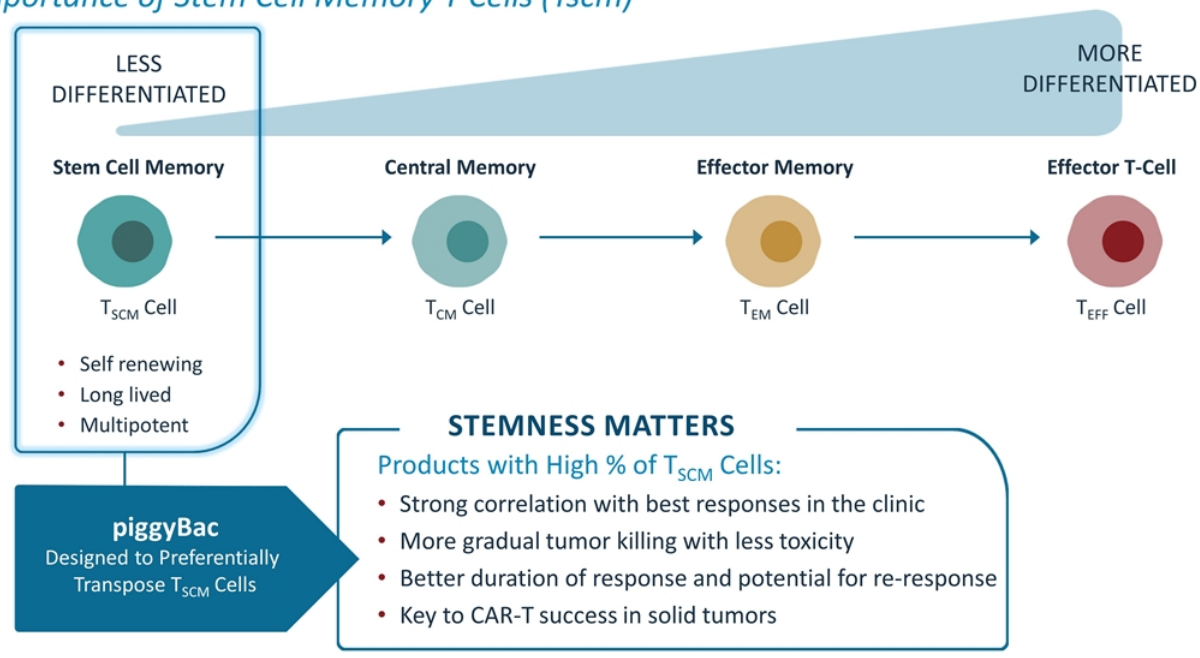
Immuno-Oncology Pre-clinical Allogeneic CAR-T Programs

Devon J. Shedlock, Ph.D.
SVP, R&D

Not All T-Cells are Created Equally

The Importance of Stem Cell Memory T Cells (Tscm)



piggyBac
Designed to Preferentially Transpose T_{SCM} Cells

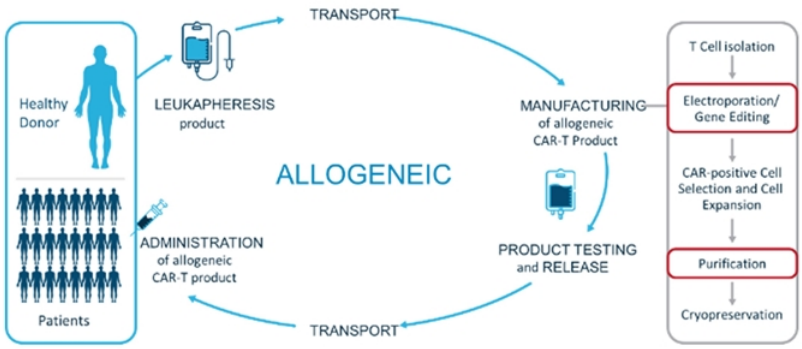
STEMNESS MATTERS

Products with High % of T_{SCM} Cells:

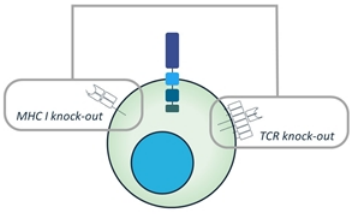
- Strong correlation with best responses in the clinic
- More gradual tumor killing with less toxicity
- Better duration of response and potential for re-response
- Key to CAR-T success in solid tumors

Poseida's Allogeneic CAR-T Platform Offers Many Unique Benefits

Allogeneic Platform Incorporates Learnings From Autologous Experience



FULLY ALLOGENEIC:
Multiplex gene editing to address graft vs host (safety) and host vs graft (persistence)



Unique Allogeneic Platform

- Preserve/improve **high T_{SCM}**
- **Optimized dosing** regimens
- **Healthy donor** material
- **Robust manufacturing**
- Dramatic **cost reductions**
  - Up to **100s of doses**

Booster Molecule

Our patented technology is designed to overcome the "Allo Tax" and **significantly increase production yield** while **preserving desirable T_{SCM} attributes** of P-BCMA-ALLO1

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P-BCMA-ALLO1

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Multiple Myeloma: An Iterative Approach to BCMA Targeting

Learning from Autologous with Focus on Allogeneic and Beyond

MULTIPLE MYELOMA – OUR POSITIONING

Multiple Product Candidates	Capacity to Cure	Importance of T_{SCM}	Focus on Tolerability	Addressing the Cost Barrier

P-BCMA-101 → **P-BCMA-ALLO1** → **DUAL (BCMA/CD19) ALLO**

Key Learnings from P-BCMA-101

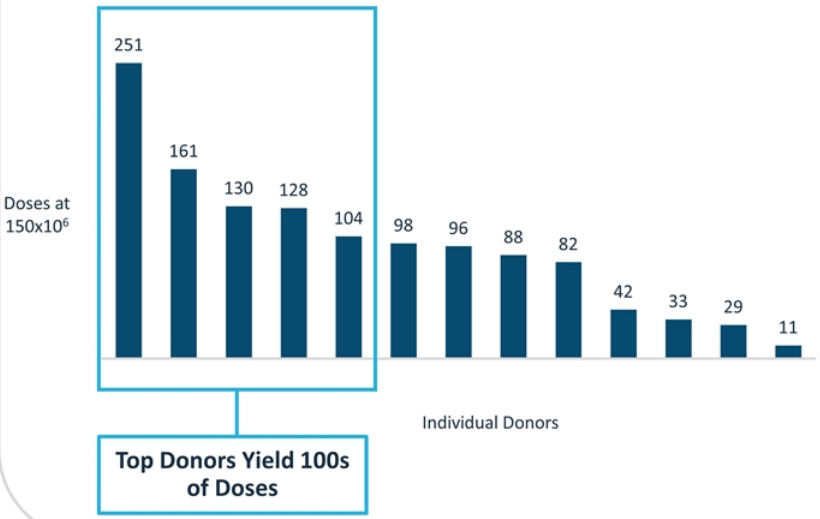
- T_{SCM} Cells are **the key**
- T_{SCM} improves **safety and tolerability** – much lower reported CRS and neurotox
- Fully **outpatient** dosing
- **Binder** choice is important
- Optimizing **manufacturing process** is critical

P-BCMA-ALLO1 and Dual (BCMA/CD19)

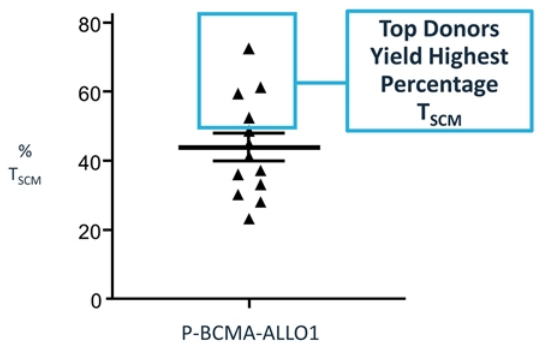
- **Preserving** T_{SCM}
- **VH Binders** for Allo and Dual CAR programs
- Booster Molecule enables **100s of doses**
- Safety, off-the-shelf convenience and low cost is an **industry game changer**
- Allo and Dual CAR approach the **next step**

P-BCMA-ALLO1: Our Booster Molecule Technology in Action

Increase Fold Expansion of CAR-T



Preserve High % of T_{SCM} Cells



- **Overcomes the "Allo Tax"**

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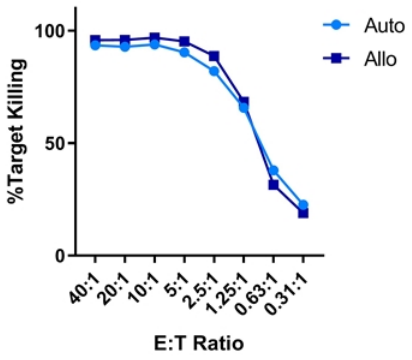
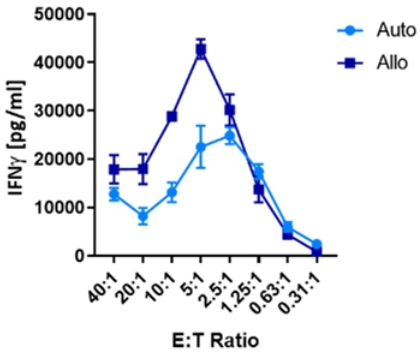
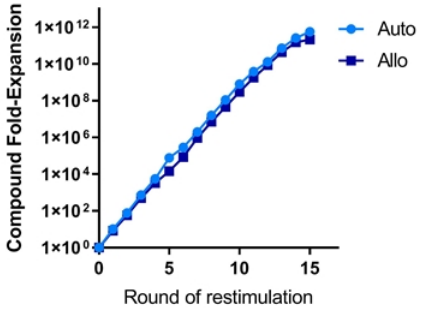
P-BCMA-ALLO1 Showed Equal or Better Results than an Autologous Version in vitro

Potent Target Cell Killing & Cytokine Secretion



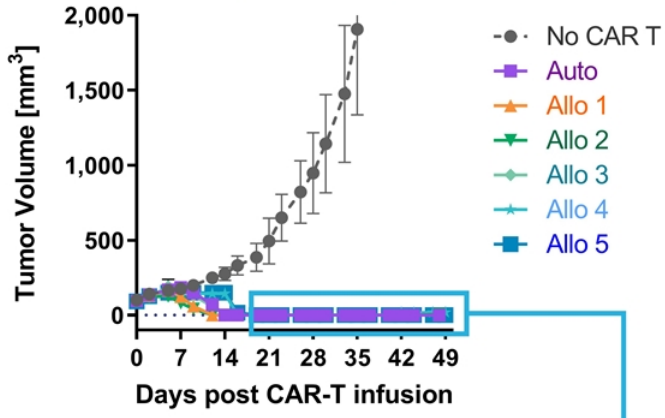


High Proliferative Capacity



P-BCMA-ALLO1 Showed Equal or Better Results than an Autologous Version in vivo

Efficacy in Multiple Myeloma Cancer Model (RPMI-8226)

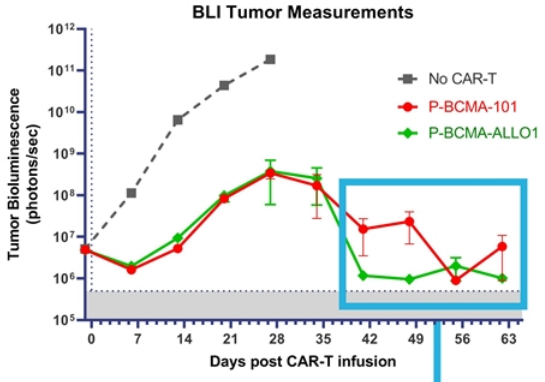


100% Tumor Elimination After ~3 Weeks

- **P-BCMA-ALLO1** was comparable to P-BCMA-101 (non-edited) CAR-T
  - **complete tumor elimination**
  - **similar CAR-T cell expansion**
- This stringent model has been **fine-tuned using P-BCMA-101 clinical samples** with known outcomes
  - **100% positive predictive value**: If clinical product completely killed tumor in the animal model, then it also had excellent activity in the clinical trial

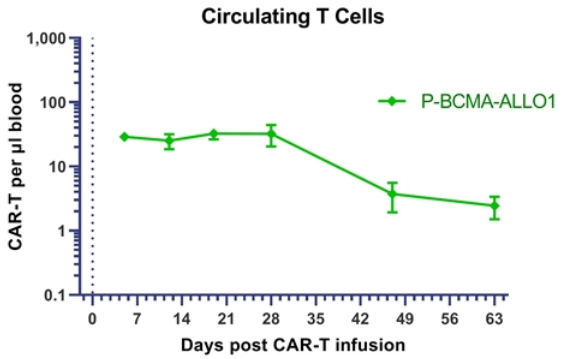
P-BCMA-ALLO1 Demonstrates Tumor Control and Durability in a Challenging MM1S Preclinical Model

Tumor Control



Tumor Relapse Control at Standard Dose

In Vivo Durability



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P-MUC1C-ALLO1

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Stem Cell Memory T Cells Key to CAR-T Success in Solid Tumors

Multiple Product Candidates in Solid Tumor Indications

CONVENTIONAL PERCEPTION

Poor CAR-T responses in solid tumors to date with T cell products comprised of maturated effector T cells, but some complete responses if **multiple doses are administered**

OUR APPROACH

Our product candidates have a high percentage of **T_{SCM} cells**, which hold the potential to engraft, self renew and **create wave after wave of effector cells with one administration**

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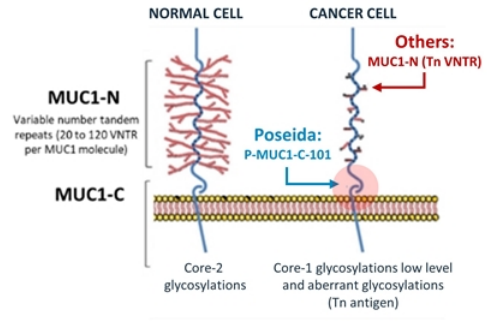
P-MUC1C-ALLO1: Allogeneic Solid Tumor Program with Broad Potential

Our Approach vs Others

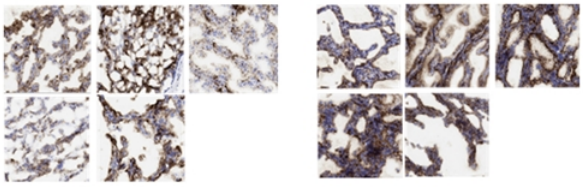


- MUC1 is highly polymorphic and normally expressed on apical surface of epithelium
- On cancer cells, an aberrant form is expressed, and polarity is lost
- P-MUC1C-ALLO1 epitope may be tumor-specific and is retained on the cell surface following cleavage of MUC1-N

Tumor Type	Total MUC1 Expression (%)*	Poseida MUC1C IHC frozen tissue data (%)**
Breast	91	92
Ovarian	83	93

**American Cancer Society, 2017; **Positive samples defined as: Frequency: + - occasional cells, ++ - few cells, +++ - many cells Intensity: 2 - mild, 3 - moderate, 4 - heavy staining*

Breast **Ovarian**



- **P-MUC1C-ALLO1** potentially addresses patient populations in **multiple solid tumor indications** including many epithelial-derived cancers
  - Breast, Ovarian, NSCLC, Colorectal, Pancreatic and others
- **High Representation of P-MUC1C-ALLO1 Epitope** in Breast and Ovarian Cancer

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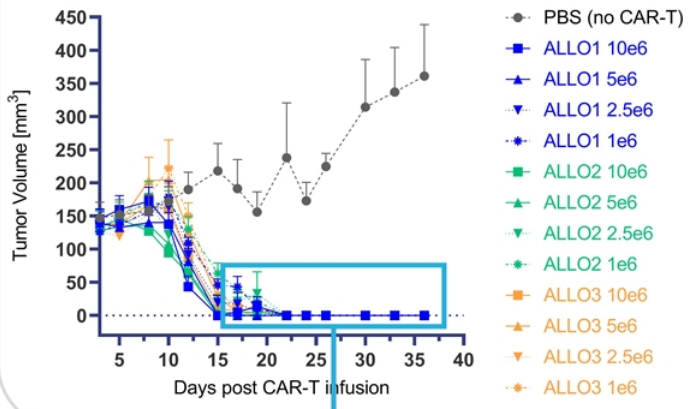
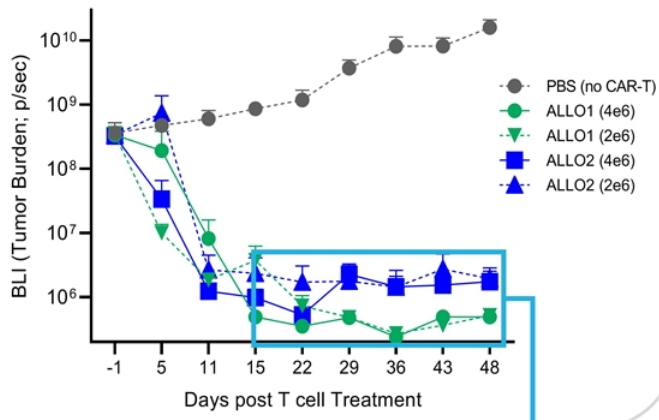
P-MUC1C-ALLO1 CAR-T Demonstrated Potent In Vivo Activity

TRIPLE-NEGATIVE BREAST (MDA.MB.468) AND OVARIAN CANCER (OVCAR3) MODELS

Triple-Negative Breast Cancer Model



Ovarian Cancer Model



100% Tumor Elimination After ~2 Weeks

P-PSMA-ALLO1

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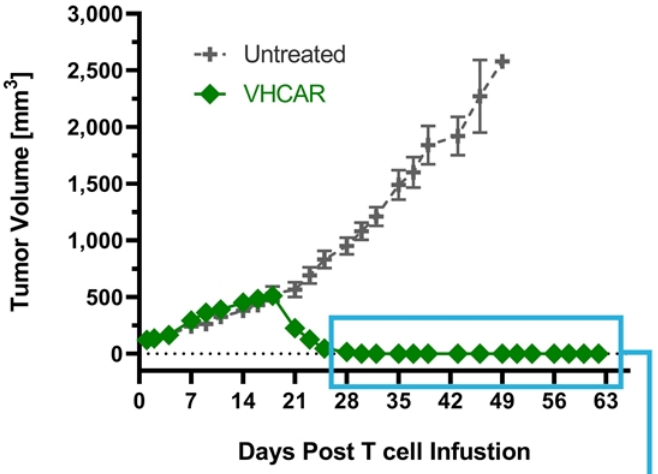
P-PSMA-ALLO1: Optimized Allogeneic Version of P-PSMA-101

- All the advantages of our fully allogenic platform
- Superior single domain (VH) binder technology (VCAR)

Efficacy of PSMA VH CAR at "Stress Test" Dose in Difficult Prostate Cancer Model (LNCaP.luc)



100% Tumor Elimination After ~4 Weeks

Dual CAR-T Programs

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The Advantages of Dual Antigen Targeting with Dual CAR T

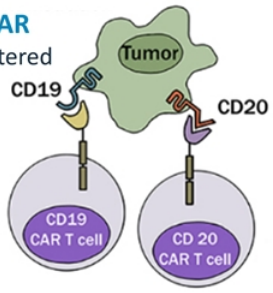
1. Overcome single antigen loss (heme)

CD19 CAR T clinical trials: 7-39% of relapse is caused by loss of CD19 antigen

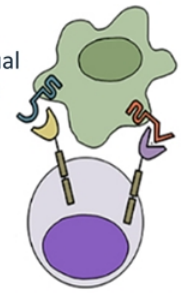
2. Target heterogeneous tumors (solid)

Highly heterogeneous antigen expression may contribute to modest CAR-T clinical responses against solid tumor

Single CAR
Co-administered



Dual CAR
Co-localized dual engagement



Tandem CAR
Conformation challenges?

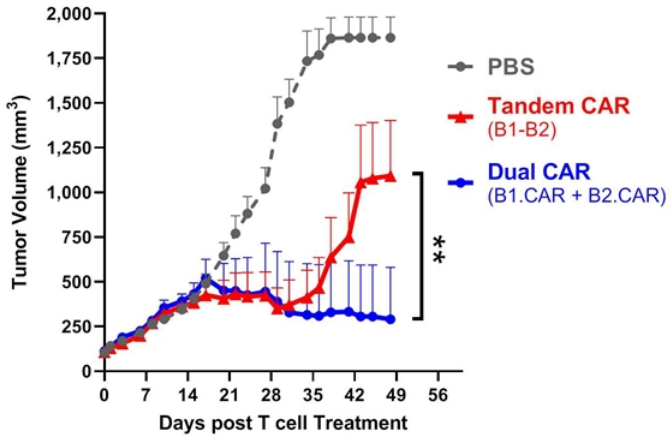
Shah et al., Front Oncol. 2019; 9: 146

Poseida's PB transposon system has large cargo capacity and can effectively deliver two individual CARs, with capacity for safety switch, selection gene (and/or others) → **Competitive advantage**

Dual CAR is More Effective In Vivo Than a Tandem CAR

- **Comparing various formats** of our single-domain VH binders:
  - Single CAR
  - Single Tandem CAR
  - Dual CAR
- We have learned:
  - A tandem CAR may be better than a single CAR
  - However, a **Dual CAR-T is always better than a single or tandem CAR-T**
- Lessons learned will be implemented in future pipeline programs

Dual CAR-T vs Single Tandem



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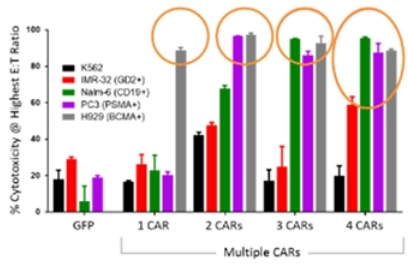
Dual-Target Allogeneic CAR-T Product Candidates

piggyBac's Large Cargo Capacity Enables the Next Wave of Opportunity

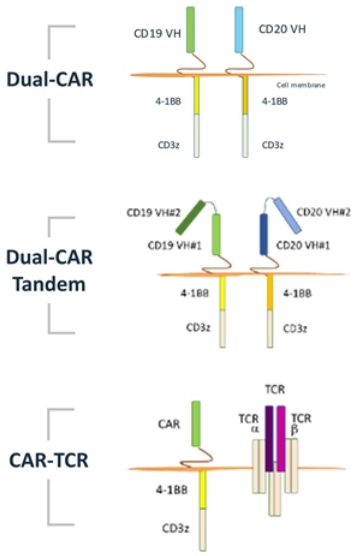
Proof of Concept



piggyBac shown to deliver 6 genes, including 4 fully functional CAR molecules plus a selection gene and a reporter gene in a single transgene

- Cargo capacity can also enable **armoring or other strategies** to drive efficacy or durability

Our Approaches Beyond Single CARs



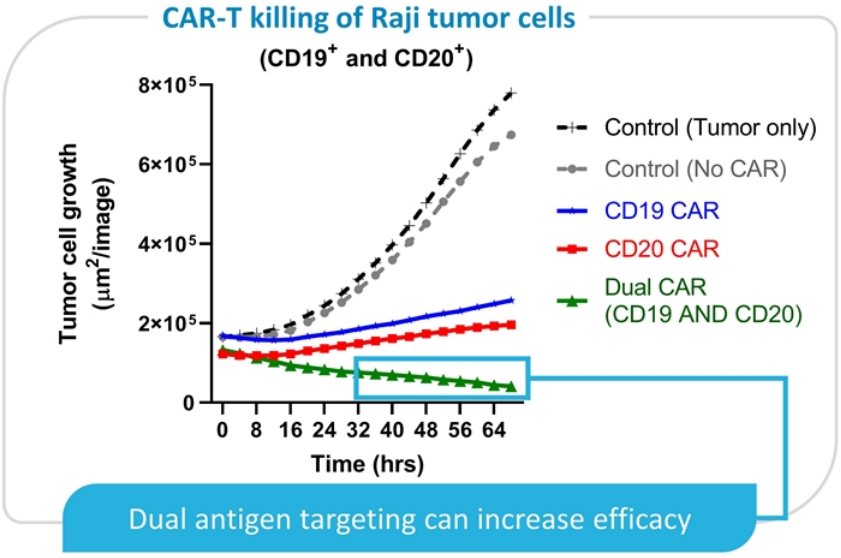
Initial Products

1. **ALLO CD19/CD20**
   B cell Leukemia and Lymphoma
2. **ALLO CD19/BCMA**
   Multiple Myeloma
3. **Dual ALLO (Undisclosed)**
   Solid Tumors

POSEIDA THERAPEUTICS

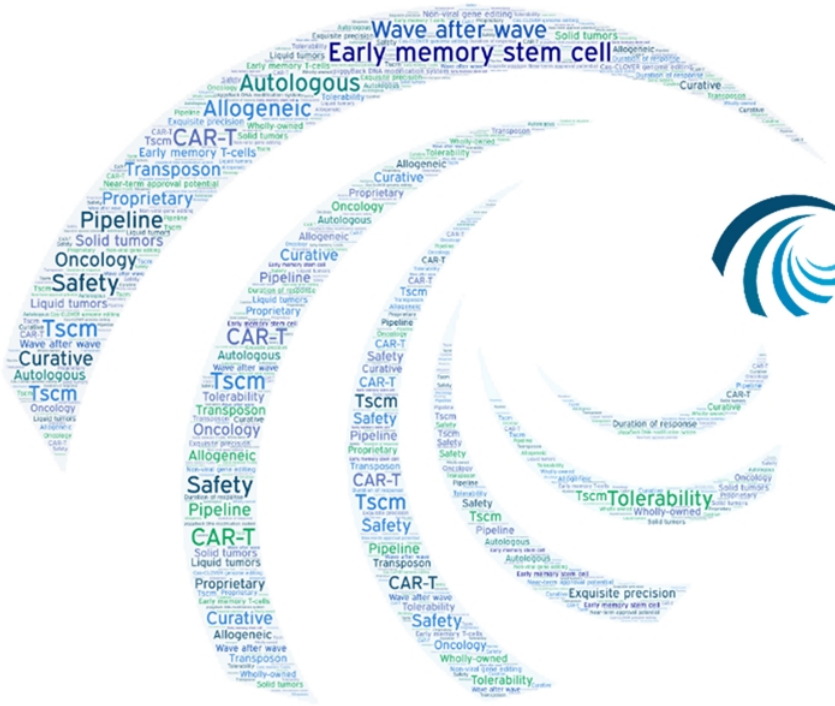
CD19/CD20 Dual CAR Program for B Cell Malignancies

- Lead optimized CD19/CD20 Dual CARs are under study
  - Quad-cistronic vectors
- Dual CAR-T maintain high % TSCM
- POC studies demonstrate Dual CARs kill (double-positive cancer cells) better than either single CAR-T alone



Summary: Immuno-Oncology Pre-clinical Allogeneic CAR-T Programs

- All programs are **fully allogeneic**, addressing both graft vs. host and host vs. graft
  - Donor selection allows for generation of products with **exceptionally high percentage Tscm**
  - **Booster molecule enables 100s of doses** from a single manufacturing run
- Pipeline candidates demonstrate **high efficacy in mouse tumor models**. Also:
  - P-MUC1C-ALLO1 has **potent activity against a wide range of human tumors**
  - P-PSMA-ALLO1 uses a **superior VH CAR (VCAR)**
  - Dual CAR-T programs are **facilitated by piggyBac's large cargo capacity**
- **INDs** in 1H 2021 (P-BCMA-ALLO1) and 4Q 2021 (P-MUC1C-ALLO1)

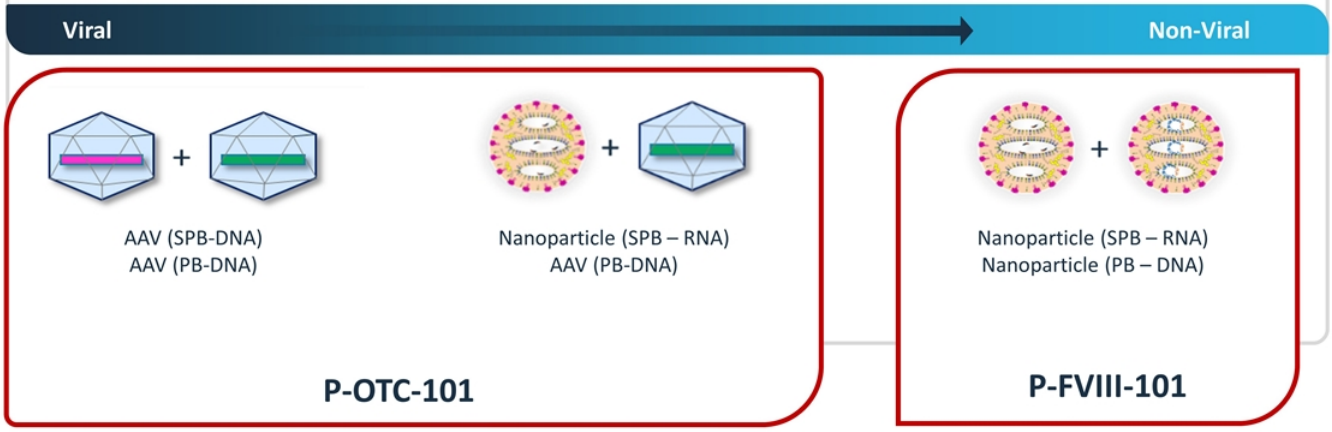


POSEIDA THERAPEUTICS

Poseida In Vivo Gene Therapy Programs

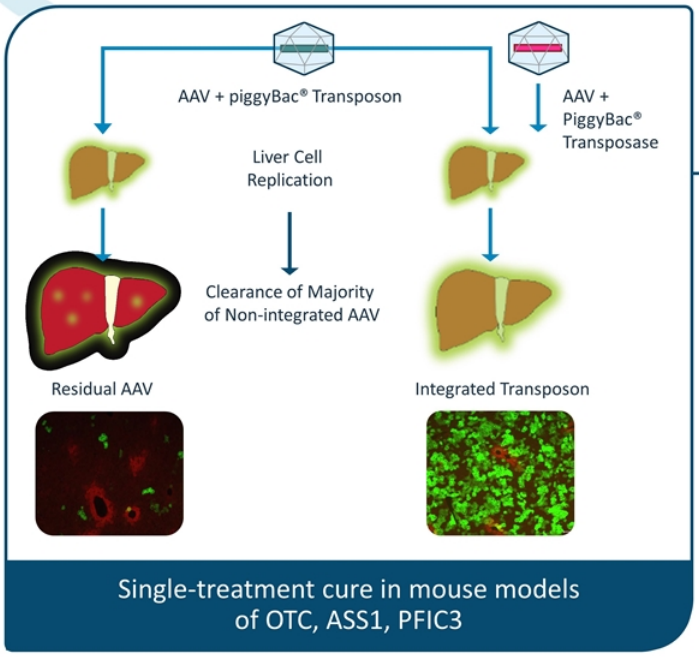
Poseida Fully Allogeneic CAR-T Approach

The goal of our in vivo gene therapy program is to enable single treatment cures of genetic diseases by combining the piggyBac® Gene Delivery System with Poseida's proprietary gene delivery platforms

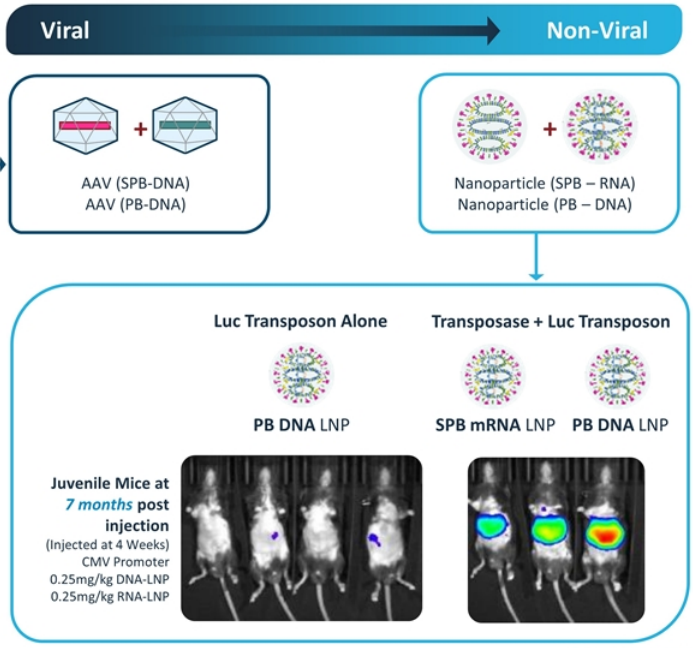


piggyBac® Changes the Game in Liver-Directed Gene Therapy

Exploring piggyBac®+AAV followed by piggyBac®+Nanoparticle



Single-treatment cure in mouse models of OTC, ASS1, PFIC3



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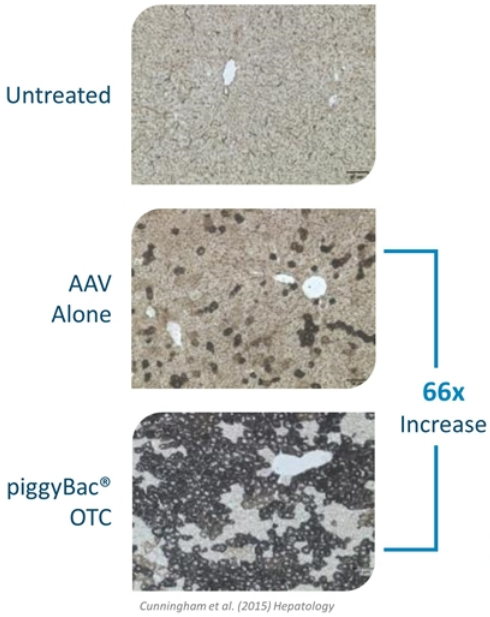
P-OTC-101 Moving Toward the Clinic

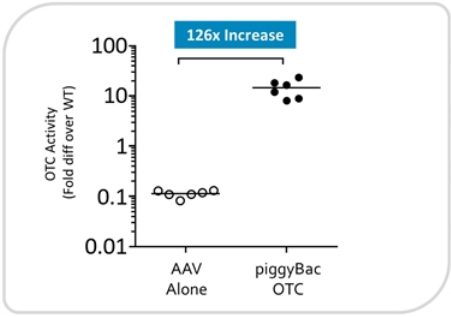
Single Injection Corrects OTC in Preclinical Model

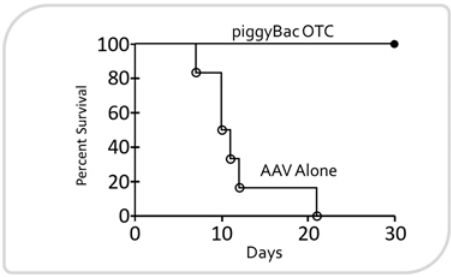
AAV (SPB-DNA)
AAV (PB-DNA)



Cunningham et al. (2015) Hepatology

- piggyBac®-based product **showed single-treatment cure in OTC mouse model** that is otherwise fatal by Day 21
- **>80% of hepatocytes permanently corrected**
- Persistence of OTC **expression observed into adulthood**
- Resulted in **126x increase in OTC levels**
  - Potential to significantly **reduce dosing**
- **All treated mice survived**





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A Single Injection of PB-ASS1 Cures Citrullinemia Type I

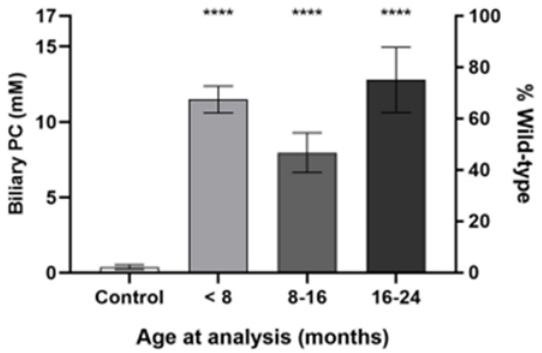
AAV (SPB-DNA)
AAV (PB-DNA)

- ASS1 -/- mice exhibit an abnormal skin and hair phenotype (left) and will die in the neonatal period if untreated.
- However, ASS1 -/- mice treated with PB-ASS1 grow hair and survive to adulthood (right)

 Cunningham et al. (2015) Hepatology

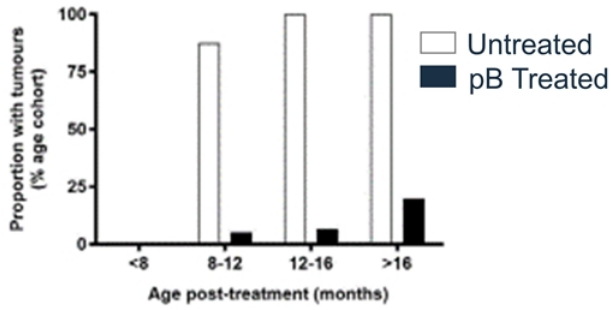
A Single Dose of PB-ABCB4 Cures PFIC3

AAV (SPB-DNA)
AAV (PB-DNA)



Across all age cohorts:

7% of PB-treated showed tumors, 95% of untreated Abcb4-/- showed tumors

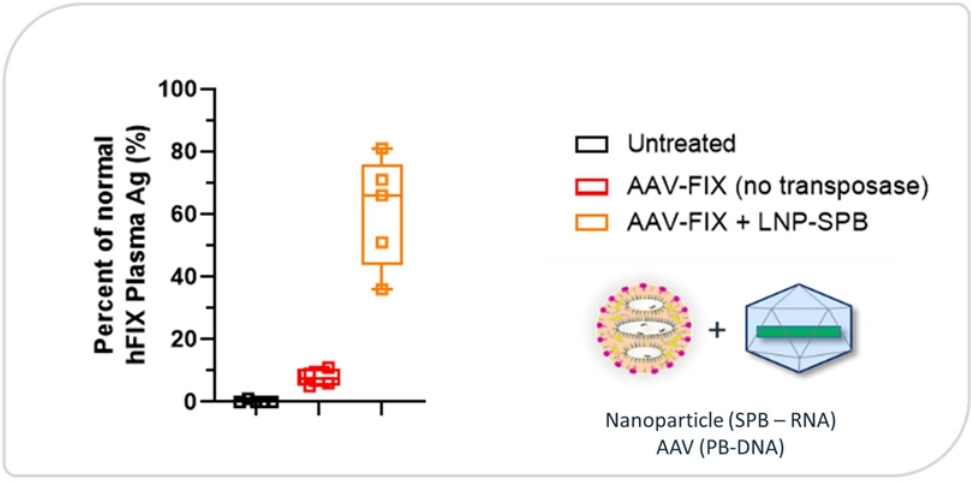


Significant reduction in incidence of macroscopic tumors* in PB-treated Abcb4-/- mice

*tumors > 1 mm

 Siew et al. (2019) Hepatology

A Single Dose of PB-FIX Results in Nearly Normal Expression Levels of hFIX



 Siew et al. (2019) Hepatology

Speakers – P-OTC-101

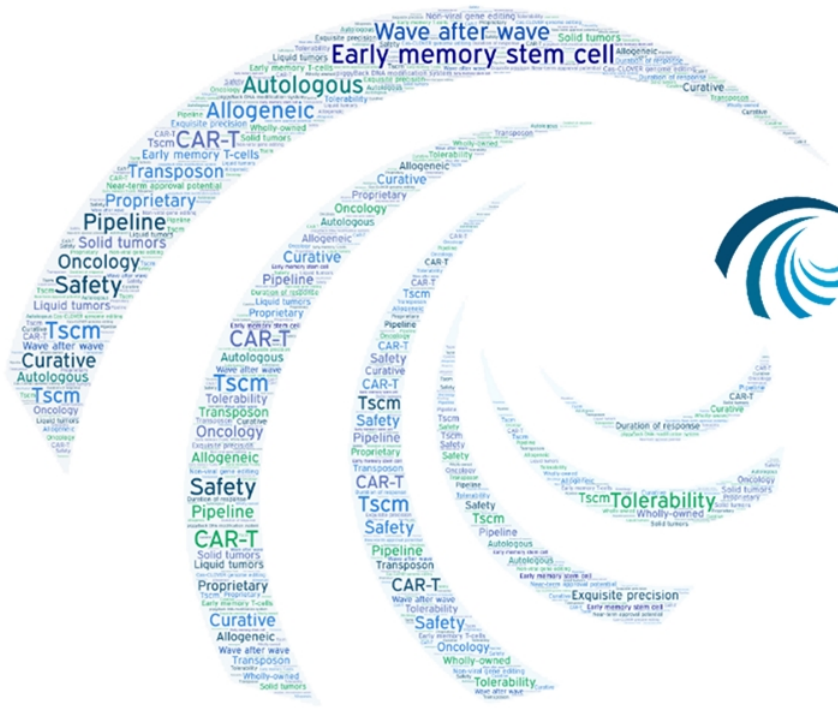
Dr. Bruce Scharschmidt, M.D.

- Former Professor of Medicine and Chief of Gastroenterology at UCSF
  - Helped start UCSF liver transplant program
- Served as Editor-in-Chief of the Journal of Clinical Investigation
  - Served as President of the American Society for Clinical Investigation
- Headed clinical development at Chiron
  - Performed first human gene therapy trial for hemophilia
- Chief Medical and Development Officer at Hyperion
  - Developed and launched Ravici for urea cycle disorders

Speakers – P-FVIII-101

Dr. Denise Sabatino, Ph.D.

- Research Associate Professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania
- Member of the Division of Hematology and the Perelman Center for Cellular and Molecular Therapeutics at The Children's Hospital of Philadelphia
- Her research focuses on factor VIII, gene-based therapeutics for hemophilia A and the immune responses to factor VIII
  - Characterization of novel FVIII variants with higher specific activity and improved secretion
  - Development of factor VIII transgenes that augment factor VIII expression
  - Studies to understand the fate of the AAV vector DNA after gene delivery



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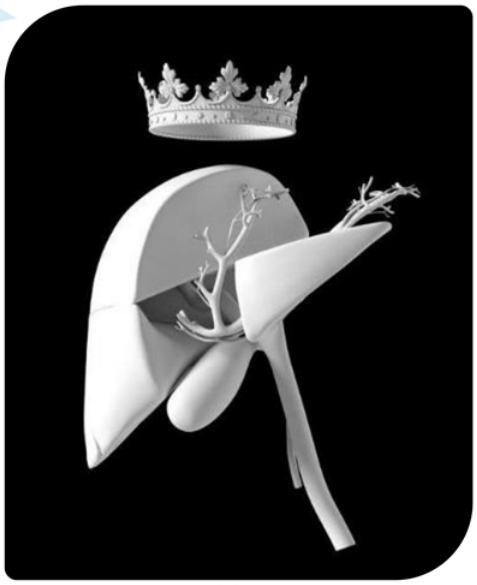
Liver Directed Gene Therapy P-OTC-101

Bruce F. Scharschmidt, M.D.

Why the Liver?



*From the **New York Times,** 2017; "The Liver: A 'Blob' That Runs the Body"*

Nutrient Metabolism & Triage

- Glycogen storage diseases
- Hypercholesterolemias / dyslipidemias
- Organic acidemias
- Amino acid disorders

Toxin Disposition

- Crigler-Najjar syndrome
- Urea cycle disorders
- Drug clearance

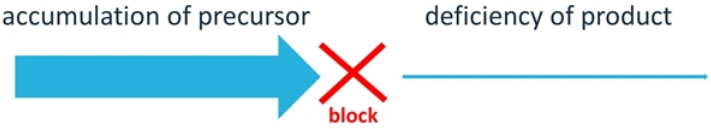
Bio-Factory

- Hemophilias (FVIII, FIX deficiency)
- Apolipoprotein deficiency
- Alpha-1-AT deficiency

Liver Diseases

- Inherited (PFIC, Wilson's)

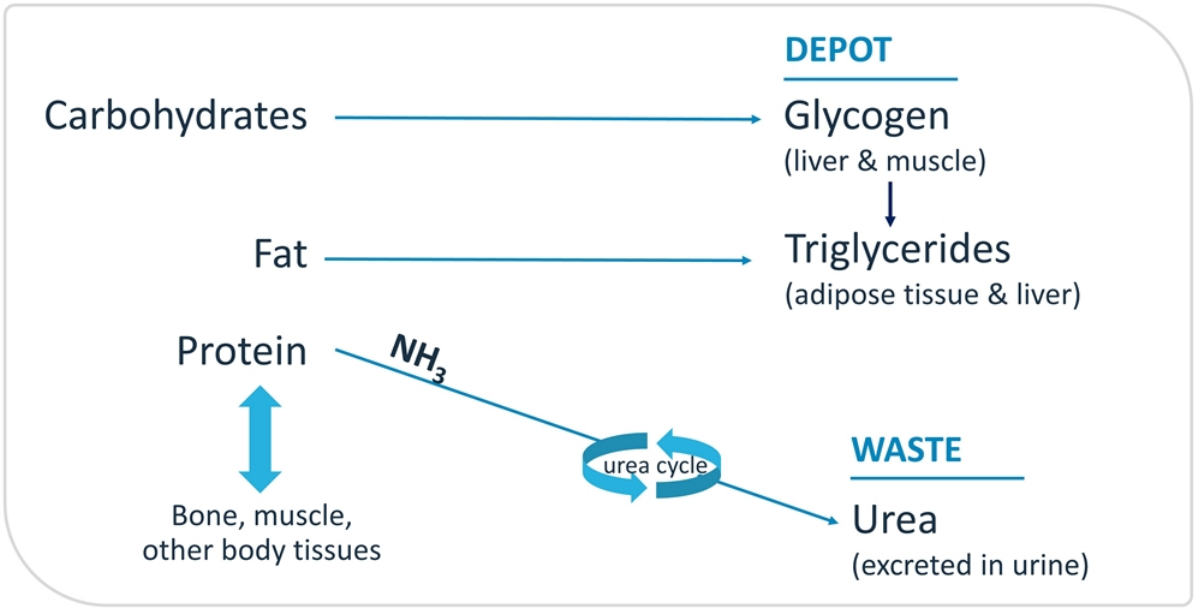
Features Common to Many Inherited Metabolic Disorders Including Urea Cycle Disorders



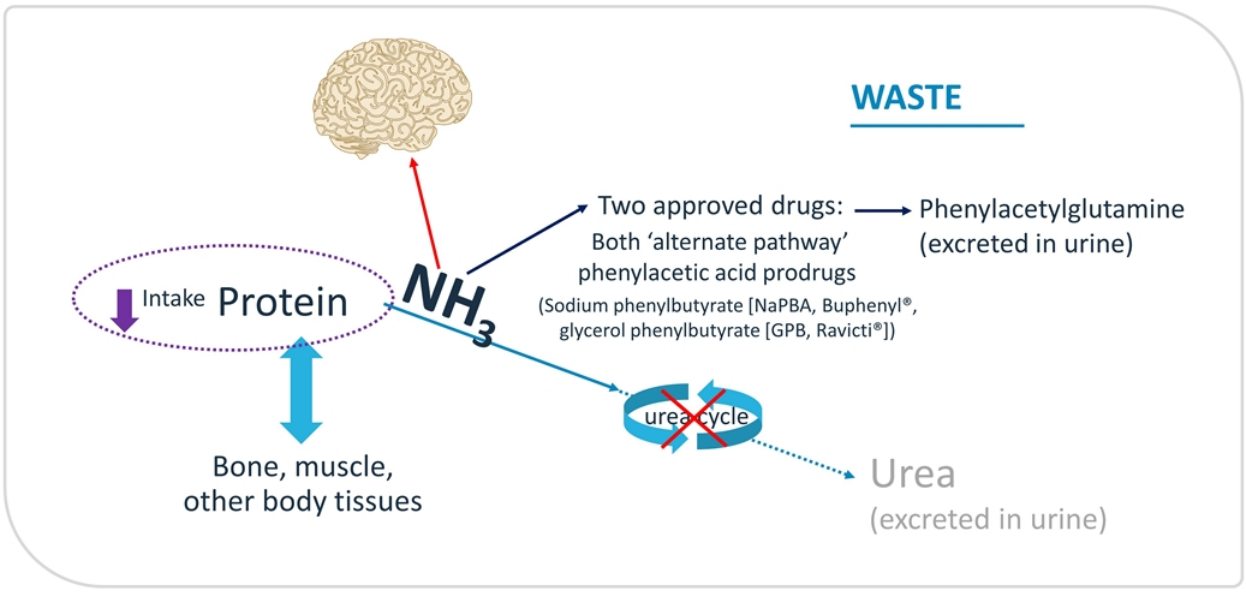
- Disease results from accumulation of upstream precursor and/or deficiency of downstream product
- Hi-fidelity / translatable dosing biomarker(s)
- Intermittent metabolic crises
- The more severe the defect, the earlier it manifests
- Diet +/- drug Rx insufficient for the most severely affected
- Major unmet need

The Human Body Has No Depot for Excess Nitrogen

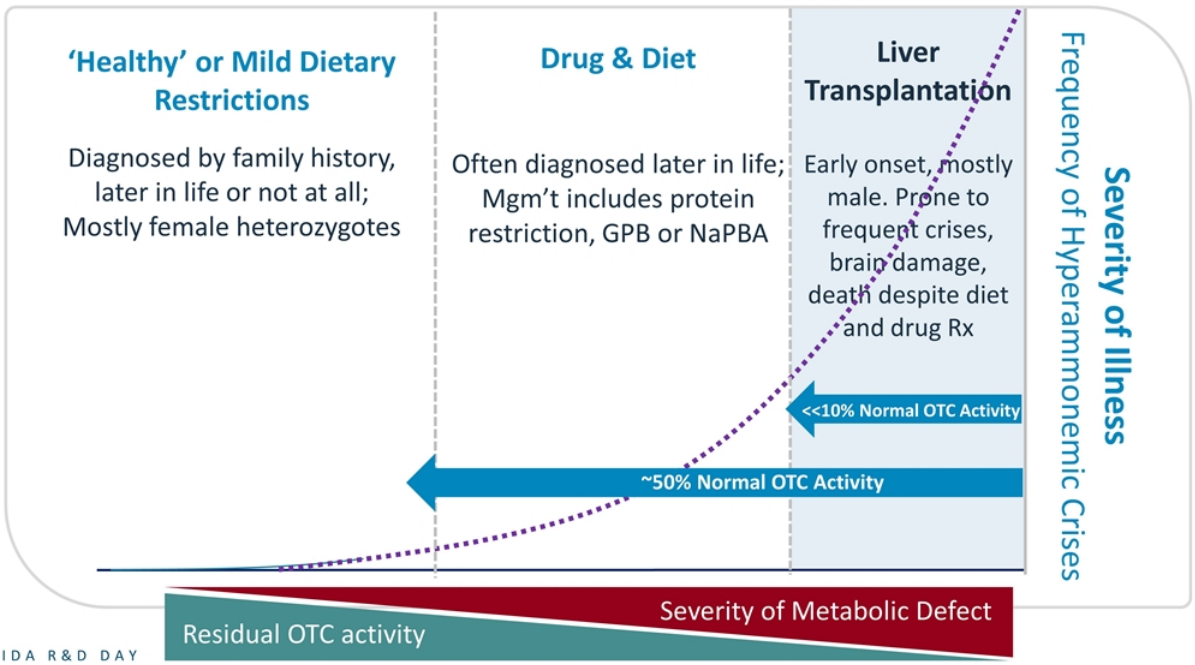
Ammonia (NH3) Resulting from Protein Catabolism is Converted to Urea and Excreted



OTC Deficiency Treatment: Dietary Protein Restriction & Alternative Pathway Drugs



X-Linked OTC Deficiency: Spectrum of Illness Ranges from Early Onset Catastrophic Illness to Asymptomatic



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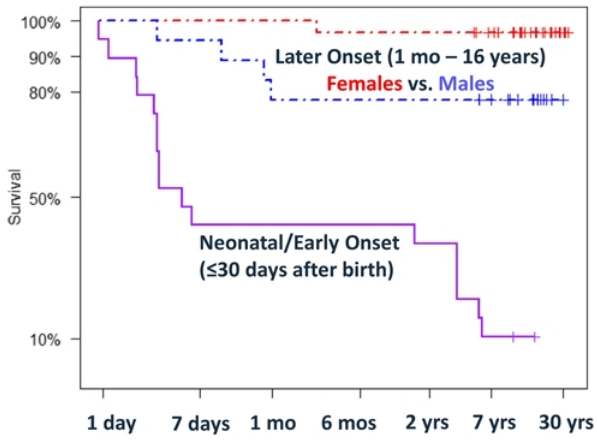
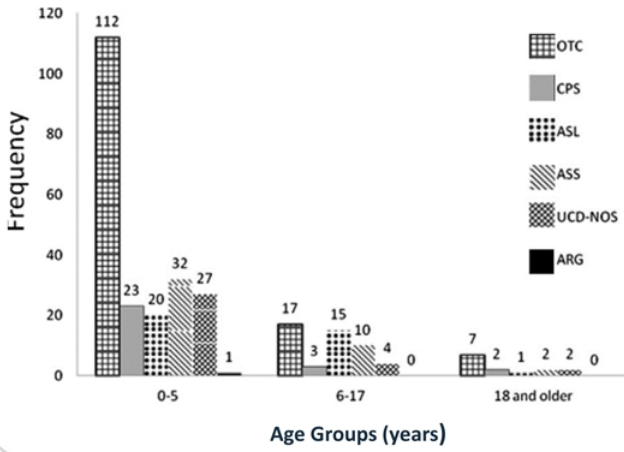
Early Onset/Severe OTC Deficiency: Major Unmet Need and Opportunity for Benefit

Survival[1]



Liver Transplantation[2,3]



1 Brassier et al., Orphanet Journal of Rare Diseases , 2015 (French series spanning 1971-2011)
2 Yu et al., Transplantation Proc., 2015 (US/UNOS liver transplant series spanning 1987-2011)
3 Haberle et al., J. Inh. Metab. Dis. 2019 (Guidelines for the diagnosis and management of urea cycle disorders)

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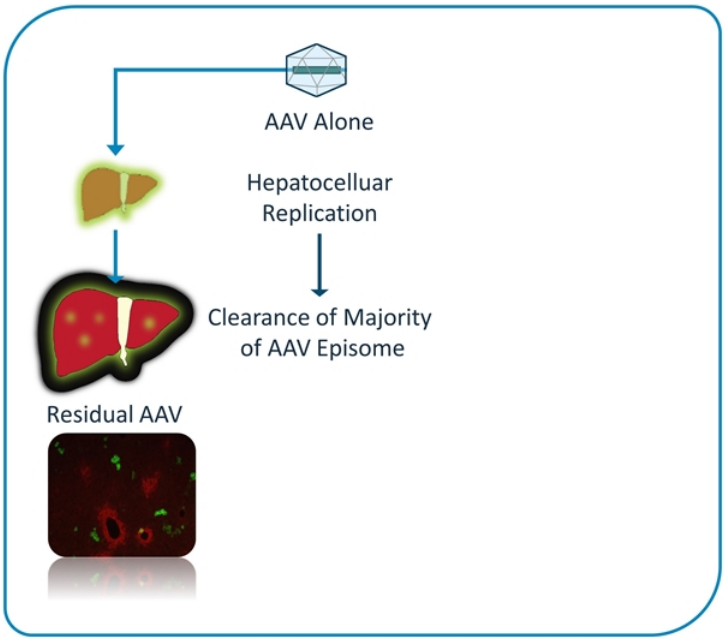
Shortcomings of Current Approaches

- AAV alone
  - Episomal, diluted with cell division
  - Not well-suited for durable, high-level expression in rapidly growing tissues
- Liver transplantation
  - Expensive
  - Inaccessible to many
  - Infants/children at risk for lethal crises while they grow sufficiently to render it feasible, or while on waiting list
  - Lifetime immunosuppression-related cost & morbidity



Cunningham et al. (2015)

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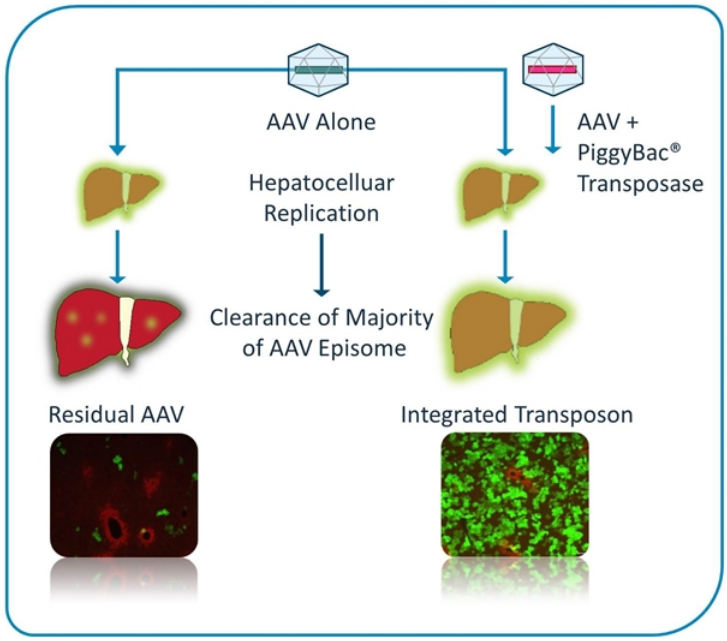
Rationale for piggyBac®

- With AAV-piggyBac®, Cunningham et al.
  - Reported single injection correction of the two UCD subtypes (OTC & ASS deficiency) usually responsible for early onset illness
  - In the OTC deficient Spf^{ash} mouse model
    - Durable, high-level transgene expression
    - Rescue of lethal phenotype
    - OTC activity increased up to 100x
  - Reported single injection correction of a genetic cholestatic liver disorder affecting infants and young children (PFIC3)



Cunningham et al. (2015)

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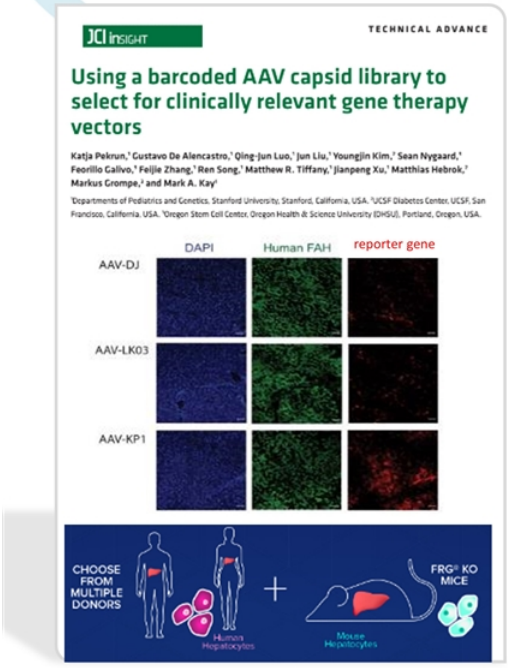
AAV Tropism in Murine and Human Hepatocytes - KP1

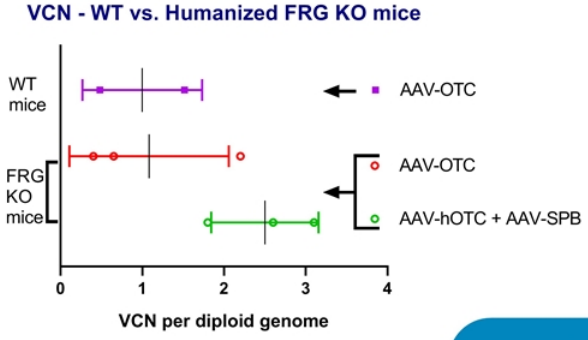


JCI insight TECHNICAL ADVANCE

Using a barcoded AAV capsid library to select for clinically relevant gene therapy vectors

Katja Pekrun,[1] Gustavo De Alencastro,[1] Qing-Jun Luo,[1] Jun Liu,[1] Youngjin Kim,[1] Sean Nygaard,[1] Feorillo Gallvo,[1] Feijie Zhang,[1] Ren Song,[1] Matthew R. Tiffany,[1] Jianpeng Xu,[1] Matthias Hebrok,[1] Markus Grompe,[2] and Mark A. Kay[1]

[1]Departments of Pediatrics and Genetics, Stanford University, Stanford, California, USA. [2]UCSF Diabetes Center, UCSF, San Francisco, California, USA. [3]Oregon Stem Cell Center, Oregon Health & Science University (OHSU), Portland, Oregon, USA.



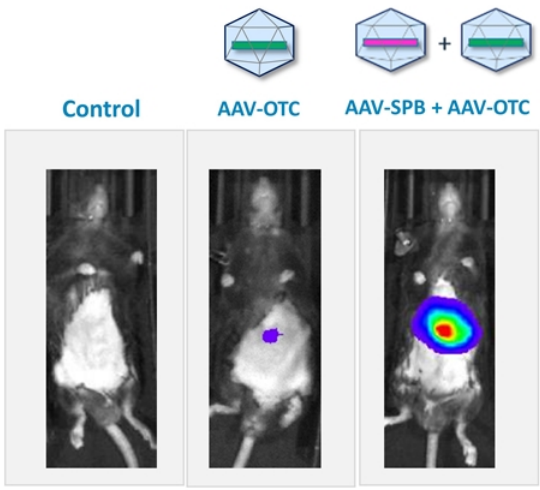
KP1 selected as lead capsid

- Infects mouse hepatocytes in vivo
- Infects primary human hepatocytes *in vitro*
- Comparable VCN between FRG KO humanized and WT mice livers
- Favorable neutralization profile

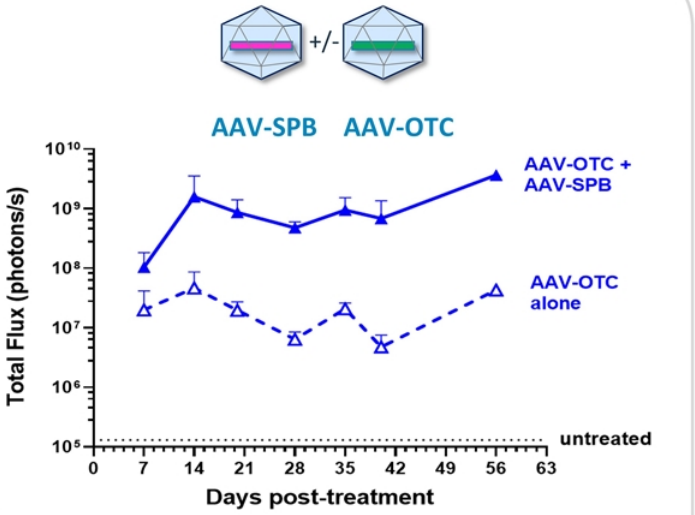
POSEIDA THERAPEUTICS

SPB Enhances Transgene Expression in Growing Liver

Liver Bioluminescence



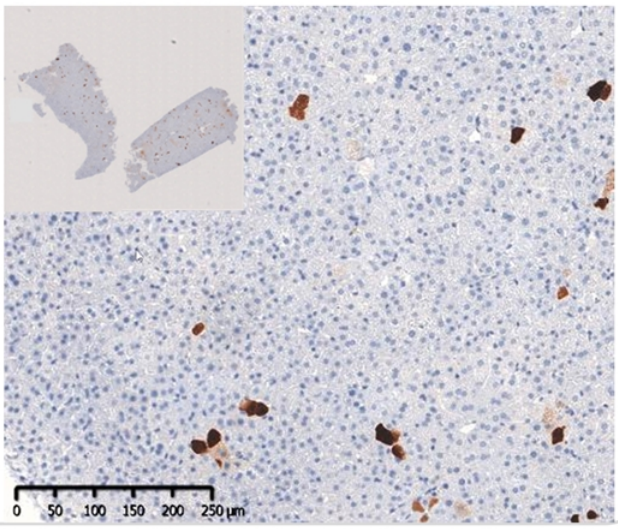
Liver Bioluminescence



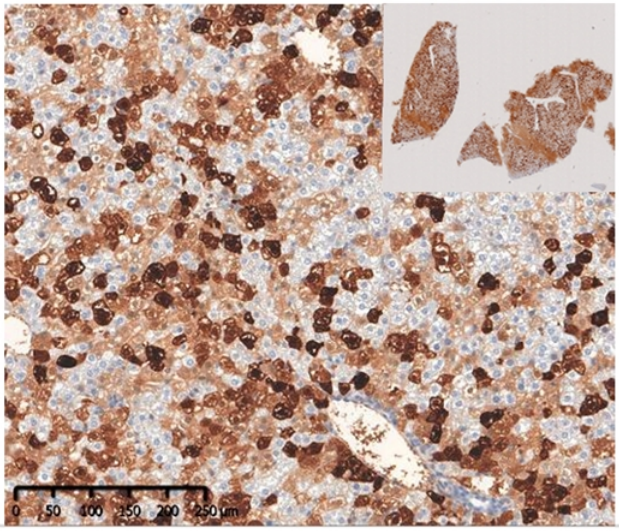
POSEIDA THERAPEUTICS

SPB Enhances Transgene Expressing Hepatocytes in Growing Liver

AAV-OTC reporter alone

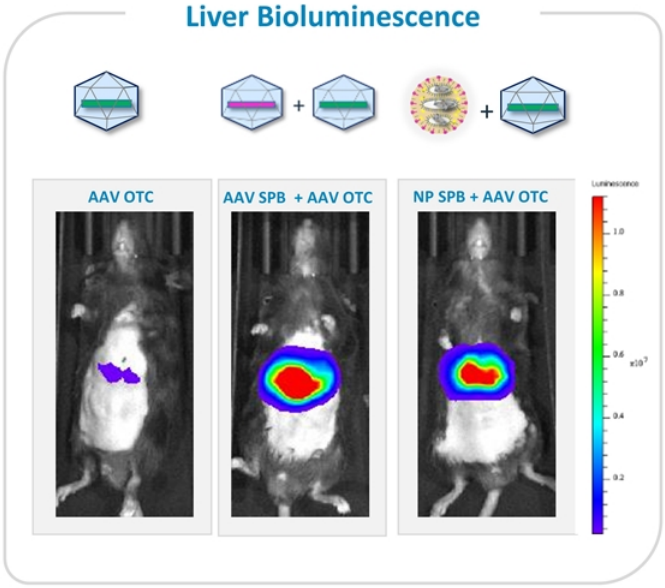


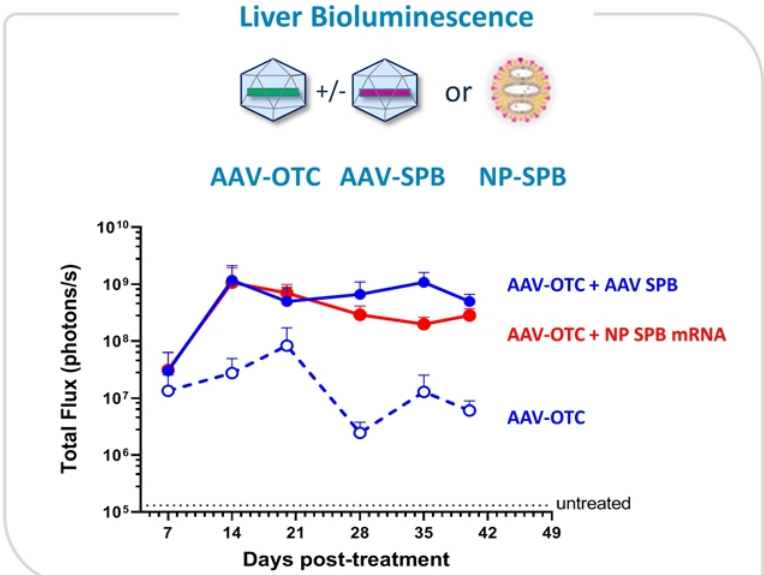
AAV-OTC reporter + AAV-SPB



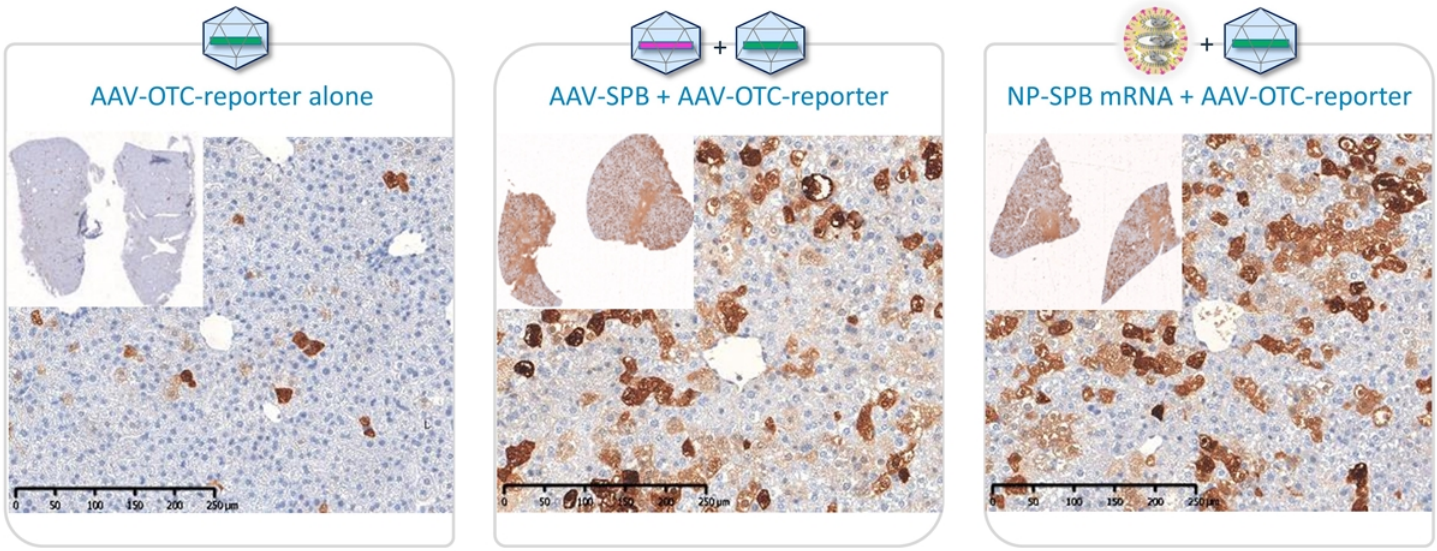
POSEIDA THERAPEUTICS

Comparable SPB Enhancement of Transgene Expression in Growing Liver with AAV or NP Delivery



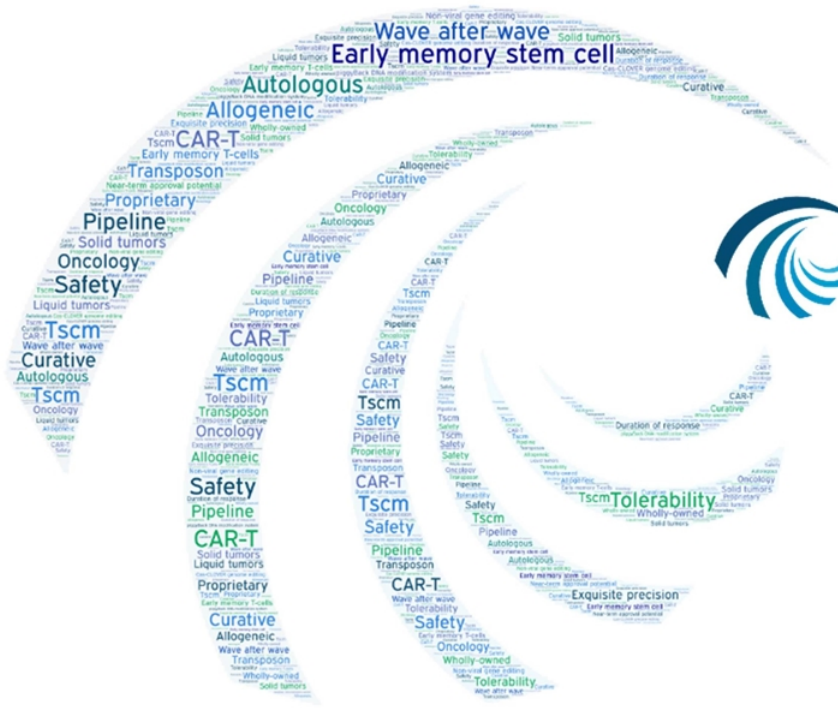


Comparable SPB Increase in Transgene Expressing Hepatocytes in Growing Liver with AAV or NP Delivery



piggyBac® for OTC Deficiency

- IND in 2022
- Platform validation for AAV-piggyBac® combination with any AAV capsid/system
- Validation for single treatment cure approach for pediatric metabolic (and other) diseases



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Nano-PB FVIII for Hemophilia A

Denise Sabatino, Ph.D.
Research Associate Professor
The Children's Hospital of Philadelphia
The University of Pennsylvania

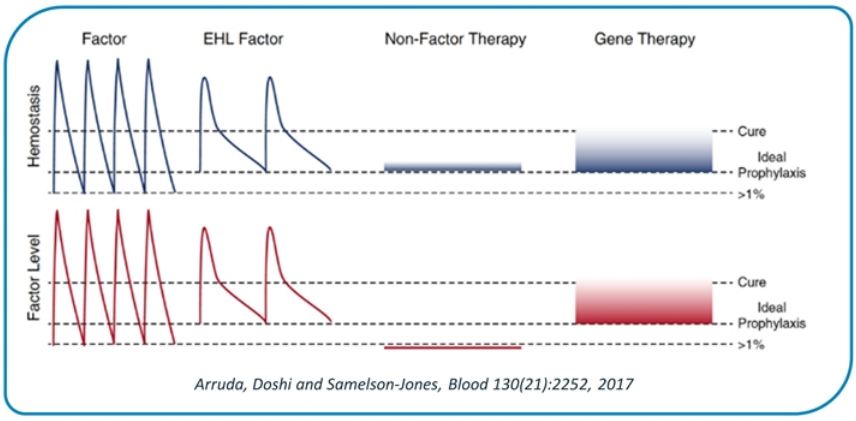
Hemophilia

- An X-linked bleeding disorder caused by a deficiency in factor VIII (hemophilia A) or factor IX (hemophilia B)
- Prevalence at birth is 1/5000 males worldwide
- 80% of affected individuals have hemophilia A
- Frequent bleeding episodes
  - Characterized by frequent spontaneous bleeding episodes, mostly into soft tissues and joints.
  - Bleeds into joint spaces results in cartilage fibrosis, loss of joint space and arthropathy
- FVIII activity correlates with the severity of the disease

Severity Classification	FVIII Activity	Bleeding Tendency	Bleeding frequency	Relative Incidence of Cases (%)
Severe	<1%	Frequent spontaneous bleeding	Weekly	50%
Moderate	1-5%	Some spontaneous bleeds; bleeding after minor trauma	Monthly	30%
Mild	>5-40%	Bleeding with significant trauma or surgery	Potentially never	20%

Current Treatments for Hemophilia

- Protein replacement therapy
  - Plasma derived or recombinant FVIII; Extended half-life FVIII
  - Requires frequent infusions of protein
  - Average annual cost of protein products is $125,000-400,000 [1]
- Non-factor based therapy --Emicizumab (Hemlibra)
  - Bi-specific antibody that binds to FIXa and FX and mimics FVIII function
- Gene therapy



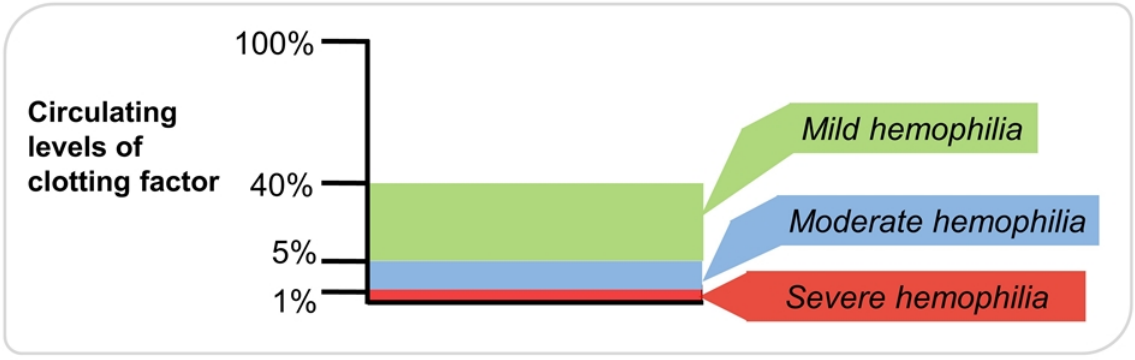
Arruda, Doshi and Samelson-Jones, Blood 130(21):2252, 2017

[1]*Croteau Haemophilia 21:285, 2015*

POSEIDA THERAPEUTICS

Goals for Novel Therapeutics for Hemophilia

- Continuous maintenance of clotting factor in circulation
- Levels of clotting factor >12% [1]
- Prevent tissue damage and improve disease phenotype
- More convenient



[1]Den Uijl et al. Haemophilia, 17(6):849, 2011

Differences Between Hemophilia A and B that Impact Development of Novel Therapeutics

	Hemophilia A	Hemophilia B
Gene	Factor VIII	Factor IX
Size of gene (cDNA)	186 Kb (7.1 Kb)	34 Kb (2.8 Kb)
Concentration of Protein in Circulation	0.1 μg/ml	5 μg/ml
Patients with inhibitory antibodies to the protein	25-30%	5%

Adeno-associated Viral (AAV) Mediated Gene Therapy for Hemophilia

- Limited cargo size (4.7 kb)
  - Challenging to use AAV for large transgenes, e.g., factor VIII
- Pre-existing immunity to AAV through natural infections
  - ~40% of population has anti-AAV antibodies that excludes them from current clinical studies
  - CD8 T cell responses to the AAV capsid can result in a loss of transgene expression due to the elimination of transduced cells; transient immune suppression can mitigate loss of transgene expression
- Re-administration is not feasible due to development of anti-AAV antibodies after initial vector administration
- AAV primarily remains in an episomal form and does not integrate
  - Episomal forms can be diluted out upon cell division
  - Important consideration for treating pediatric patients
    - ~25% of hemophilia patients are under the age of 10
- Promising clinical data in multiples studies but unknown if expression will be long lasting
  - Long-term expression for up to 10 years after AAV delivery of factor IX for hemophilia B
  - Several hemophilia A studies have shown a decline in factor VIII expression after AAV delivery
- High systemic doses of AAV is associated with toxicity and fatalities in several trials for other diseases

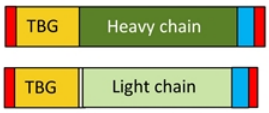
Potential for AAV Integration and Genotoxicity After AAV Gene Therapy

- rAAV predominantly non-integrating with therapeutic transgene existing as episomes.[1]
- Integration events have been observed in mice, non-human primates and humans.[2,3,4]
- In mouse models, AAV integration was associated with hepatocellular carcinoma (HCC) after delivery of AAV during the neonatal period but also in adult animals.[3,4]
  - vector dose-dependent
  - dependent on enhancer/promoter element
- HCC has not been observed in large animal models or in humans to date.

[1] *Nakai et al. J Virology 75(15):6969, 2001* [2] *Gil-Farina et al. Mol Therapy 24:1100, 2016*
[3] *Chandler et al. JCI 125(2):870, 2015* [4] Reviewed in *Chandler, Sands and Venditti, Human Gene Therapy 28(4):314, 2017*

Studies of Durability and Genetic Consequences of AAV-Mediated Delivery of Factor VIII in Hemophilia A Dogs

Two chain delivery
of canine FVIII



TBG = thyroxine-binding globulin gene promoter/enhancer

AAV Serotype	Dose (vg/vector/kg)	Total Vector Dose (vg/kg)
AAV8 or AAV9	$1.25x10^{13}$	2.5×10^{13}
	$6.0x10^{12}$	1.2×10^{13}

Hemophilia A dogs

<1% cFVIII activity

Single chain delivery
of canine B-domain deleted FVIII

hAAT = human apolipoprotein gene hepatic control region and human α-1-anti-trypsin promoter

AAV Serotype	Total Vector Dose (vg/kg)
AAV8	4×10^{13}
	2×10^{13}

Sabatino et al. Mol Ther 19(3):442, 2011
Nguyen, Everett Nature Biotechnol 39(1):47, 2020

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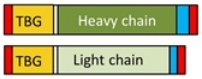
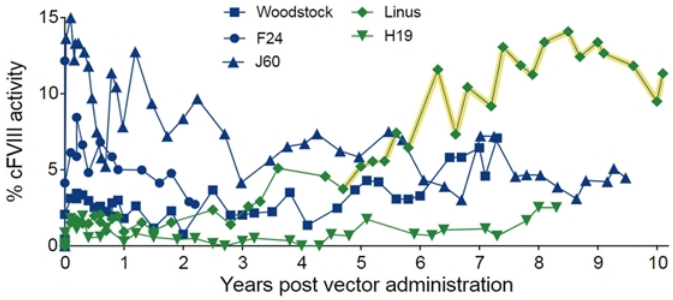
Long Term Dose-dependent Expression of cFVIII in Hemophilia A Dogs After AAV-FVIII Delivery

Two Chain Delivery

AAV8 or AAV9



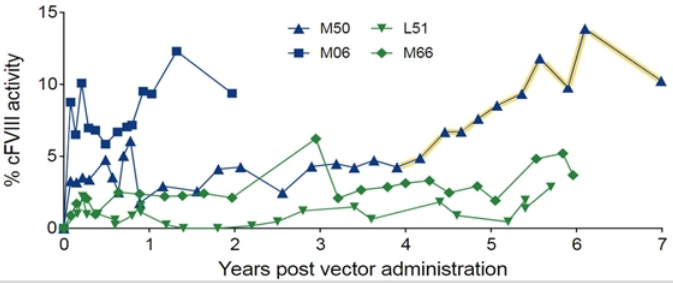
2.5×10^{13} vg/kg
1.2×10^{13} vg/kg



Single Chain Delivery

AAV8

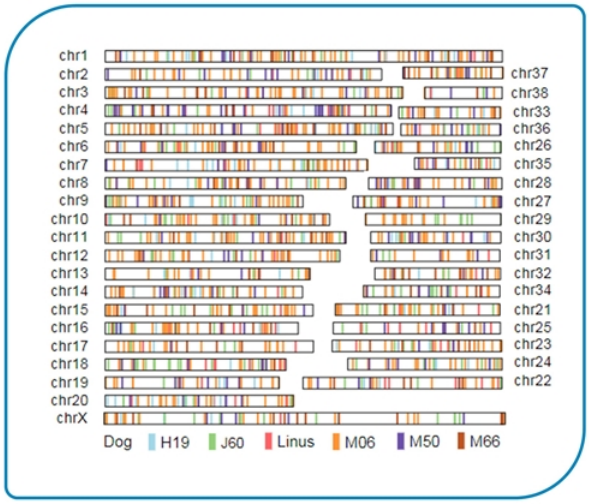
4×10^{13} vg/kg
2×10^{13} vg/kg



Nguyen, Everett Nature Biotechnol 39(1):47, 2020

DNA Analysis of AAV Genomes After Gene Therapy

- Liver samples were collected from the dogs at the end of the study for DNA analysis
- Integration events were found distributed throughout the dog genome
- Correlation between the number of AAV DNA copies and the number of integration events
- Integration favored in transcription units and oncogenes



Nguyen, Everett Nature Biotechnol 39(1):47, 2020

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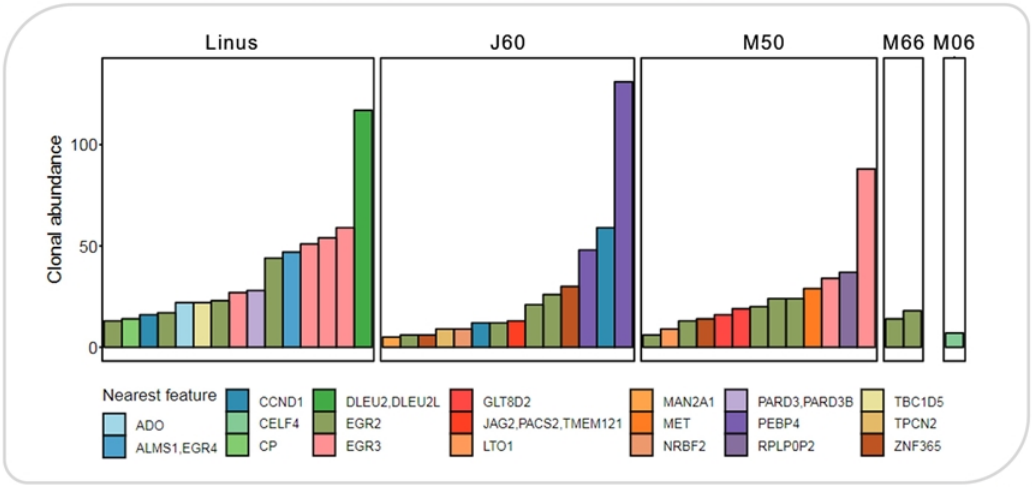
Evidence for Clonal Expansion at Sites of AAV Integration

- 54 abundant clonal populations (≥5 cells) were identified.
- Several clonal expansions had integrations near genes associated with growth control and cancers in humans.
- Sequence analysis showed that most of these integrated forms were rearranged or truncated and would not produce functional FVIII



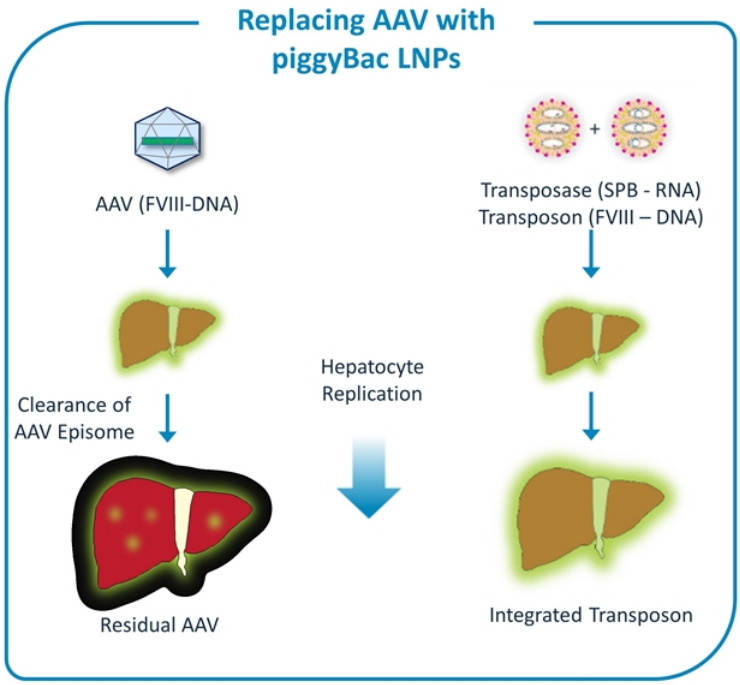
Nguyen, Everett Nature Biotechnol 39(1):47, 2020

Summary of Studies of AAV Delivery of FVIII in Hemophilia A Dogs

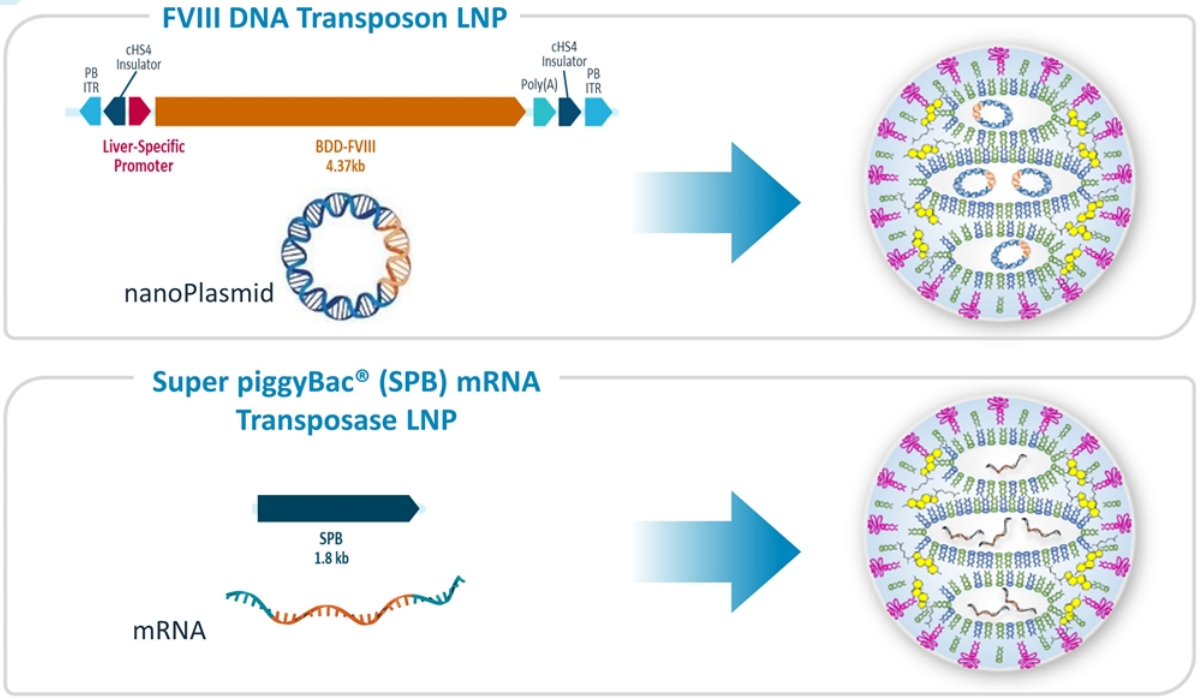
- Stable and sustained FVIII expression up to 10 years in a large animal model of hemophilia A.
- An increase in FVIII activity that was 4 times the steady state levels was observed in 2 of 9 dogs.
- While AAV integration and clonal expansion were observed, the dogs had no evidence for tumorigenesis. Hepatocellular carcinoma has not been associated with AAV in any clinical trial to date.
- A therapeutic strategy that results in stable transgene expression but without the possibility of random AAV integration would be highly desirable.

Rationale of piggyBac® Gene Modification for Treating Hemophilia

- Single treatment cure of Hemophilia A may be possible by combining piggyBac technology with nanoparticle technology, with additional advantages over AAV-based therapy:
  - No pre-existing immunity
  - No toxicity from immune response to high titer AAV
  - No toxicity from integrating AAV
  - No generation of immunity (ability to readminister)
  - Sufficient cargo capacity for desired transgene
  - Ease of manufacturing



Formulation of FVIII DNA and piggyBac® mRNA LNPs at Poseida



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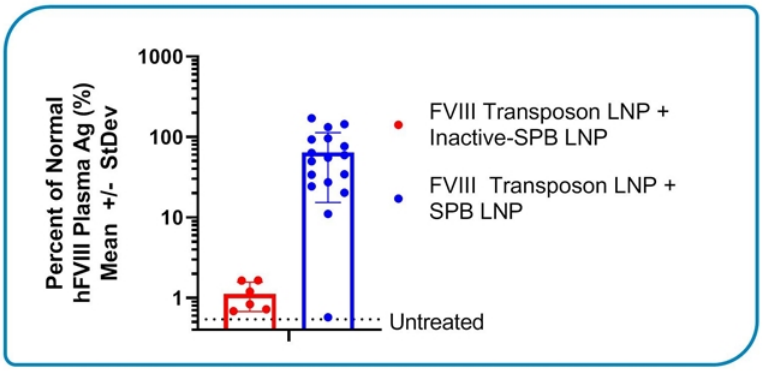
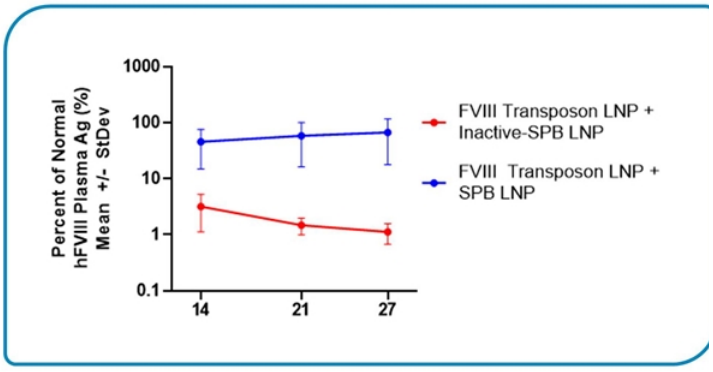
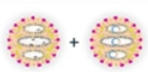
hFVIII Delivery by LNP to Newborn Mice Results in Therapeutic hFVIII Protein Levels on Day 21





- Nanoparticles encapsulating SPB mRNA and human FVIII DNA transposon co-administered IV to wild type mice on day 1 of life
- Concentration of human FVIII protein reaches 135% of normal levels
- FVIII maintained over duration of study despite dividing liver



Nanoparticle (SPB – RNA)
Nanoparticle (PB – DNA)

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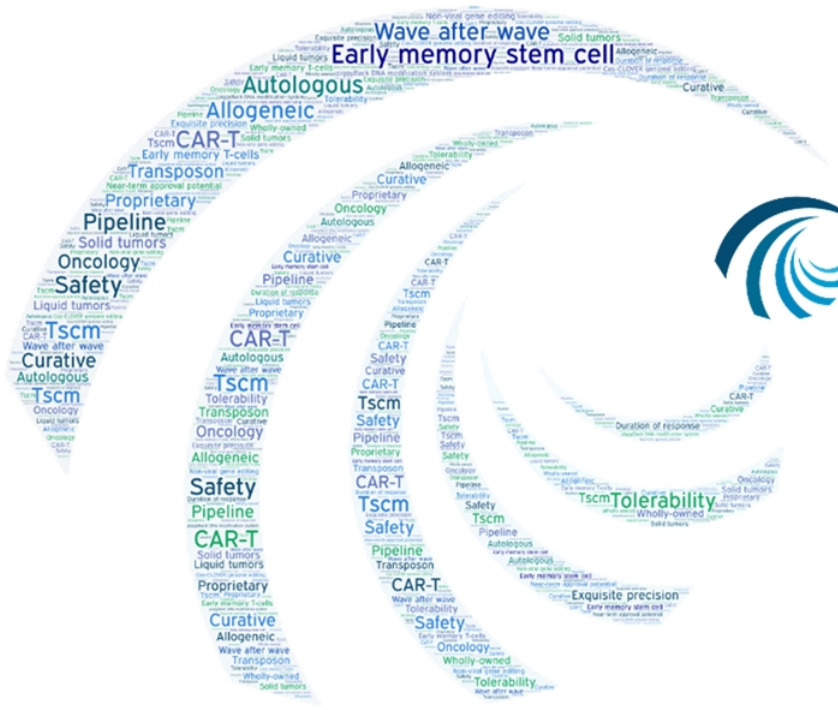
Summary

- piggyBac® gene modification delivered via lipid nanoparticle technology may provide a safe and cost-effective strategy for long-term correction of hemophilia A.
- Approach can be used in pediatric patients to achieve long-term expression without need for re-administration.
- May allow treatment of patients who have pre-existing immunity to AAV that would otherwise exclude them from current AAV-based clinical studies.



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Emerging Discovery:

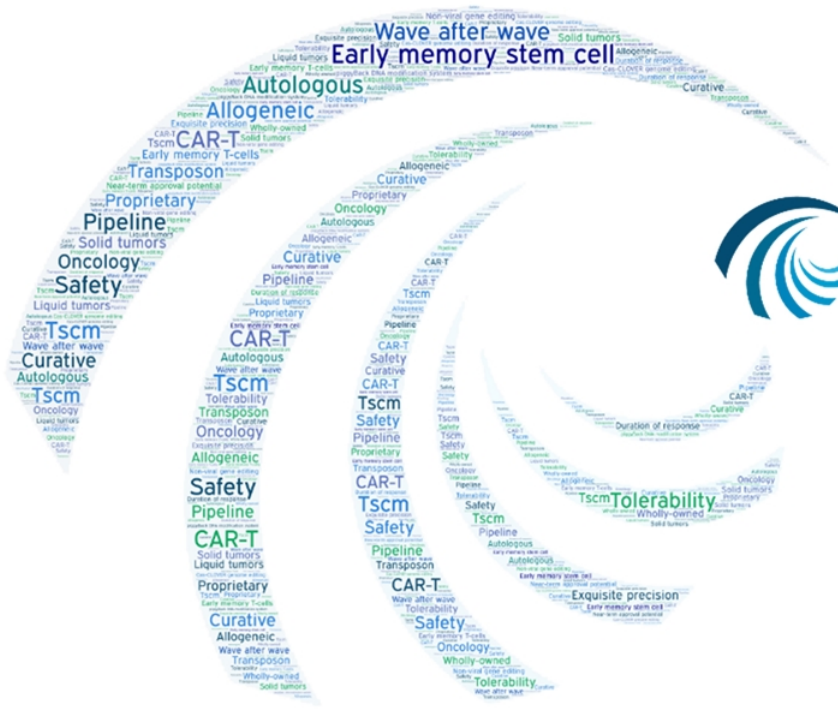
TCR-T Platform

CAR-T Outside of Oncology

HSC Platform

iPSC Platform

CAR-NK Cells for Oncology



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Poseida's TCR-T Cell Platform

Sumiti Jain, Ph.D.
Director, Immuno-Oncology

Advantages of Poseida's Allogeneic TCR-T Products

Off-the-shelf TCR-T cell product candidates, derived from healthy donors and leveraging our allogeneic CAR-T program, could treat any HLA-matched patients

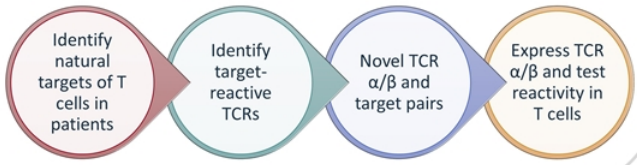
TCR-T approach may **overcome limitations** of antigen availability that CAR-T faces (by accessing intracellular antigens), expanding indications in oncology and into new areas (infectious disease, autoimmune, etc.)

TCR-T approach may be **combined with CAR-T approach**

PARTNERSHIP WITH

TSCAN THERAPEUTICS

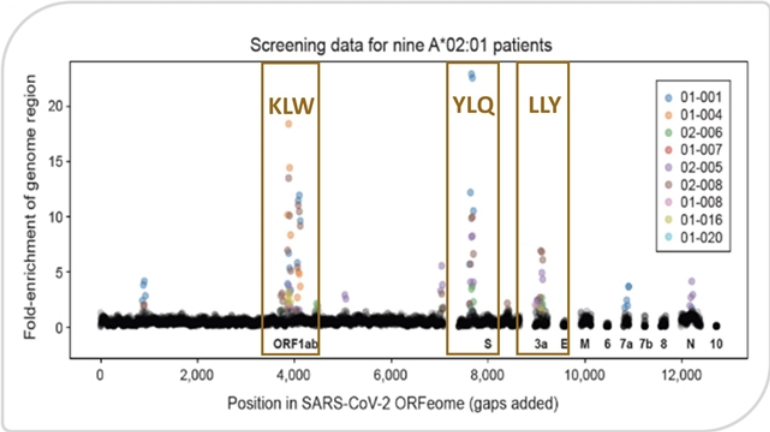
TScan platform can identify **high affinity TCRs** targeting desired immunodominant epitopes



Anti-SARS-CoV-2 Proof Of Concept

Three immuno-dominant HLA-A*02:01 restricted epitopes identified from convalescent COVID-19 patients

- Epitope-reactive TCRs identified
- TCR αβ sequences cloned
  → to be tested in engineered T cells



EPITOPE	PROTEIN	TCR αβ clones
KLWAQCVQL	ORF1ab	63
YLQPRTFLL	S (spike)	31
LLYDANYFL	ORF3a	29

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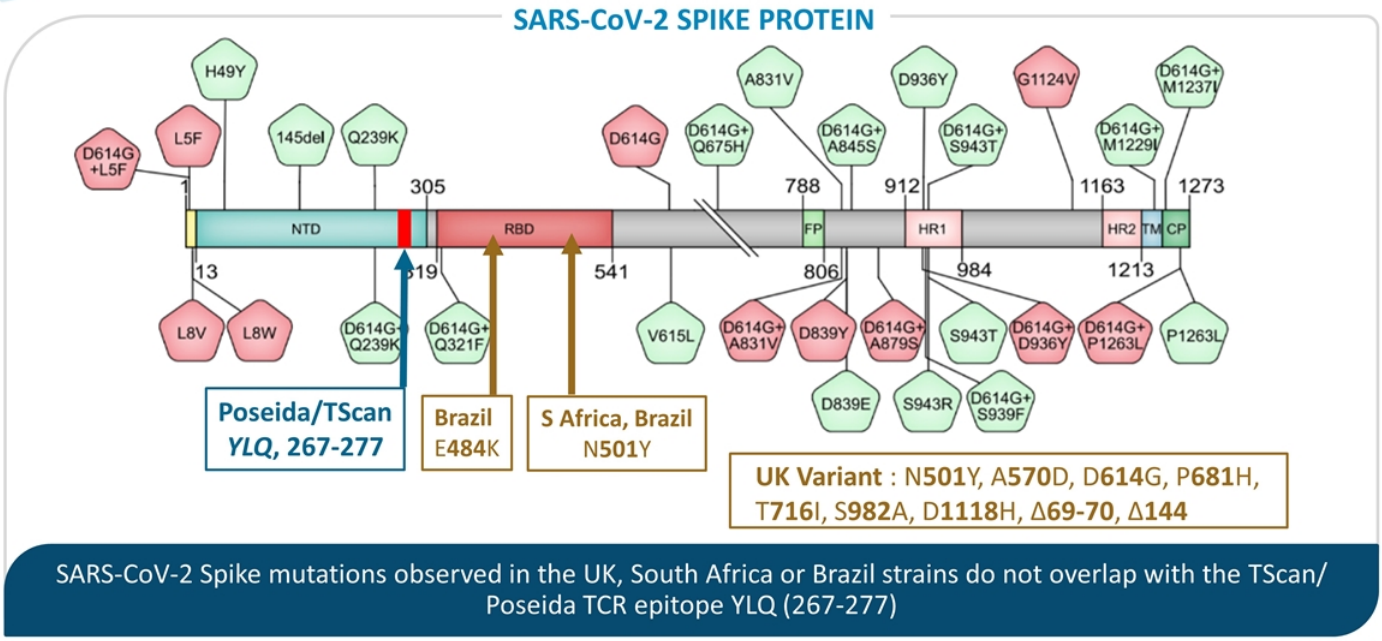
TCR-T May Be Effective Against Highly Infectious and Potentially Vaccine-resistant Emerging Mutants Of SARS-CoV-2



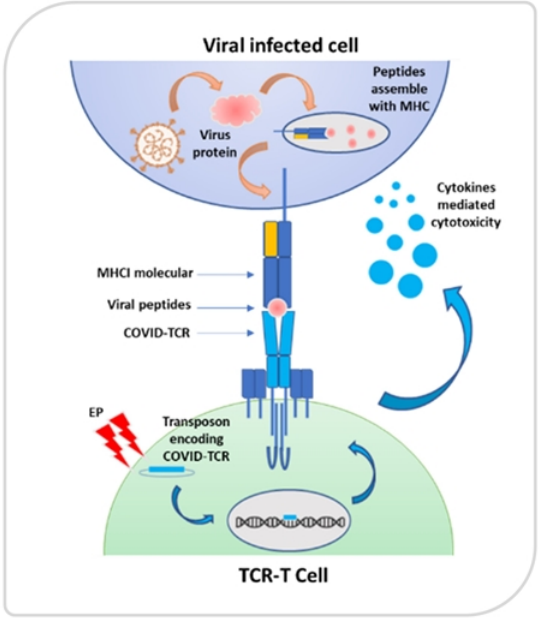
SARS-CoV-2 Spike mutations observed in the UK, South Africa or Brazil strains do not overlap with the TScan/ Poseida TCR epitope YLQ (267-277)

Identification of TCR αβ Pairs for TCR-T: Assess Epitope-Specific Activity and Functional Avidity

Screen pairs for expression and epitope specific reactivity

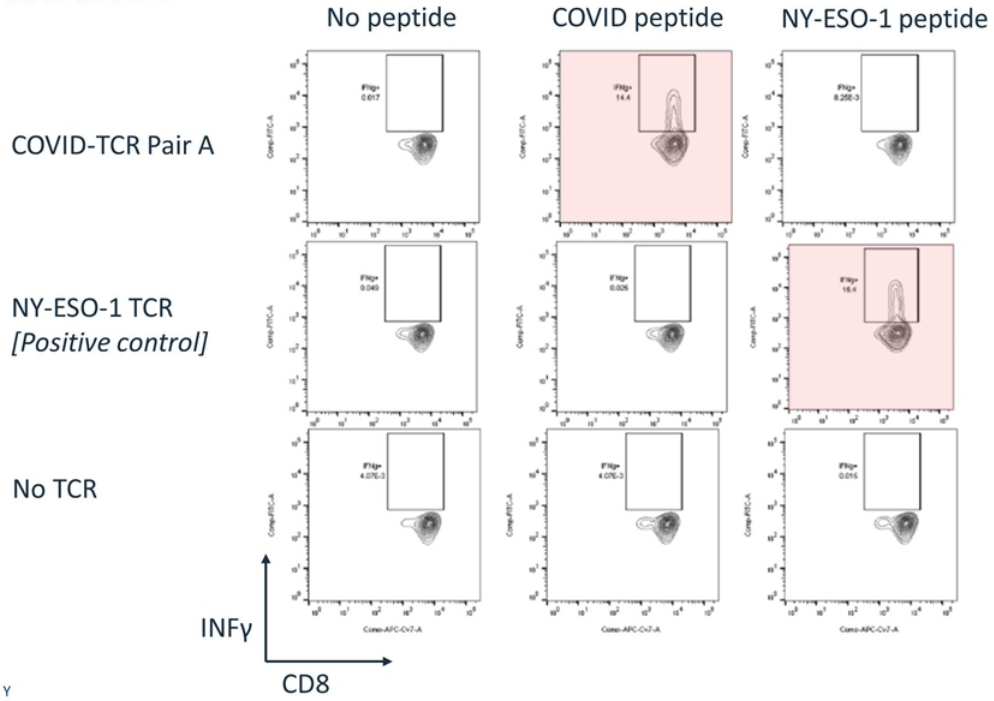
Triage for functional avidity

Generate TCR-T cells at Poseida → in vitro & in vivo testing



TCR αβ Pairs Exhibit Epitope-Specific Reactivity

Representative data shown



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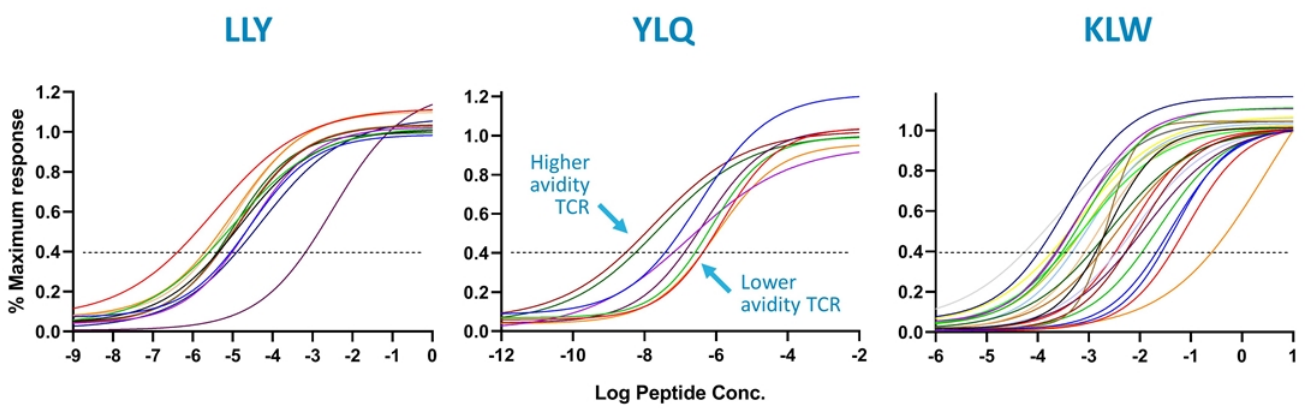
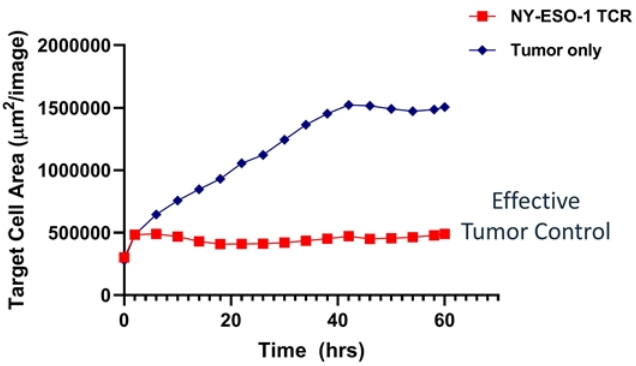
Epitope-reactive COVID TCRs Exhibit Potent Functional Avidity



PiggyBac®-Engineered TCR-T Cells are Functional in vitro and Maintain High Percentage of Desirable T_{scm} Cells

NY-ESO-1 TCR-T

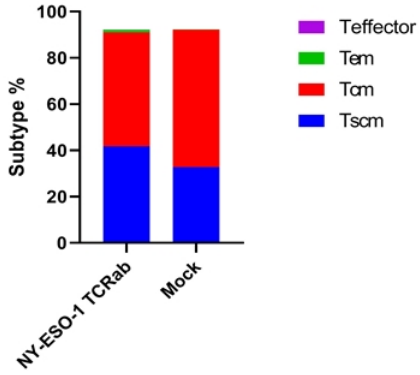
In vitro effector function against target cell



NY-ESO-1 TCR-T

Maintains % Tscm

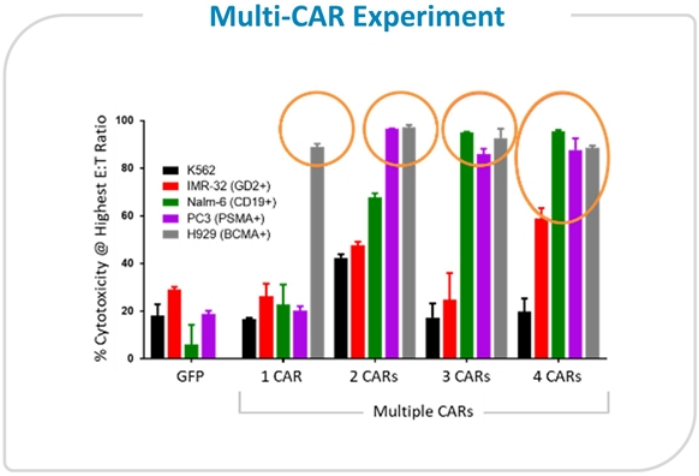
***Both Mock and NY-ESO-1-TCRαβ cells are gene-edited by Cas-CLOVER to KO endogenous TCR-β**



Combination of CAR-T and TCR-T Platforms

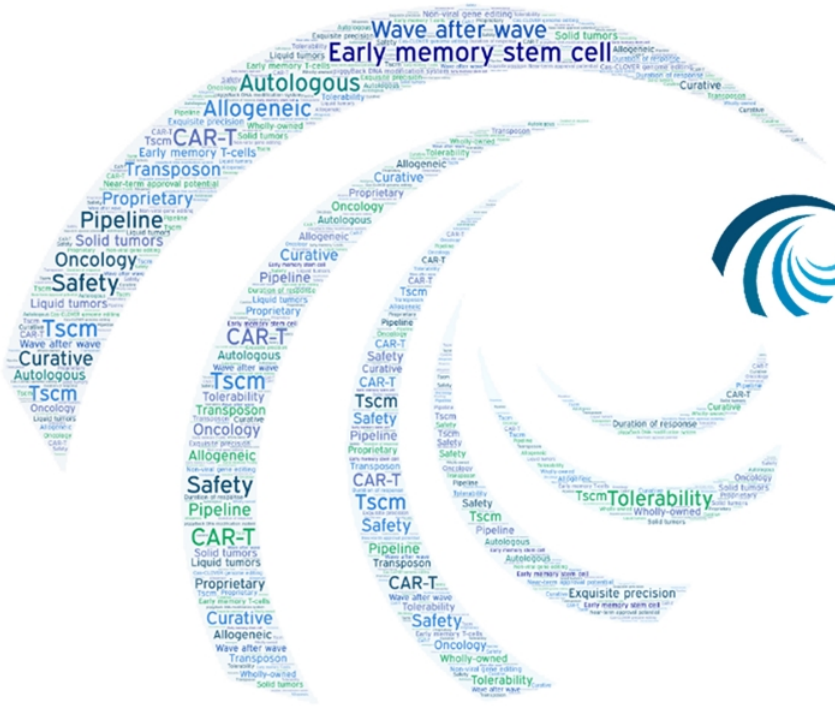
- piggyBac® technology can be leveraged to deliver target-specific CAR and TCR αβ to target both intra- and extra-cellular antigens in same product (we have already demonstrated delivery of six functional genes in a single transgene)

- Hybrid CAR/TCR-T cells may exhibit better killing and higher tumor infiltration in solid tumor indications



Summary

- Poseida's piggyBac® and Cas-CLOVER™ gene editing technologies can be leveraged to generate effective and functional off-the-shelf TCR-T product candidates with a high percentage of highly desirable T_{scm} cells
- Our TCR-T platform may be leveraged to increase the number of potential indications in oncology and allow us to expand the number of non-oncology indications (infectious diseases, autoimmunity, etc.)
- Hybrid CAR/TCR-T product candidates are enabled by the massive cargo capacity of piggyBac® and may exhibit better killing and higher tumor infiltration in solid tumor indications

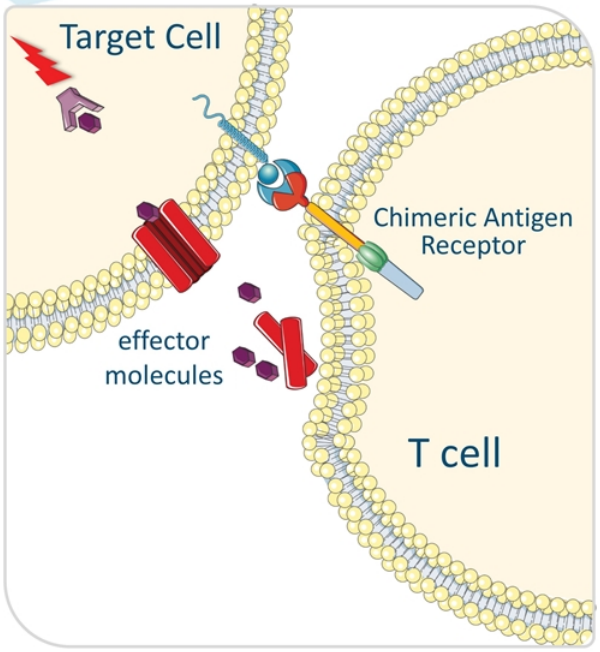


POSEIDA THERAPEUTICS

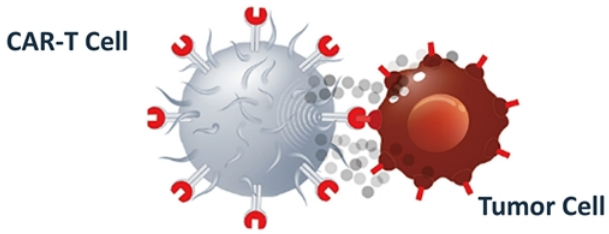
Poseida's CAR-T Platform Beyond Oncology

Nina Timberlake, Ph.D.
Associate Director, Gene Therapy

CAR-T cells: A Mechanism for Targeted Cell Removal



CAR-T cells have traditionally been targeted at tumors….

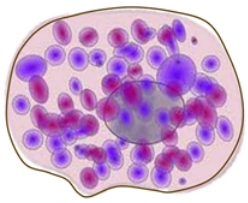


…but there are other cells in the body that may be desirable to target for killing

Reimagining CAR-T Cell Targets

Allergy/Asthma

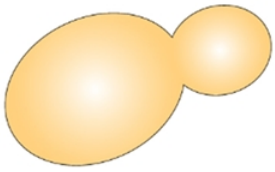
Global allergy immunotherapy market was >$2B in 2020 and rapidly expanding



Mast cell
(or other allergy-related cell)

Infectious Disease

Targeting of infected cells or directly targeting some pathogens



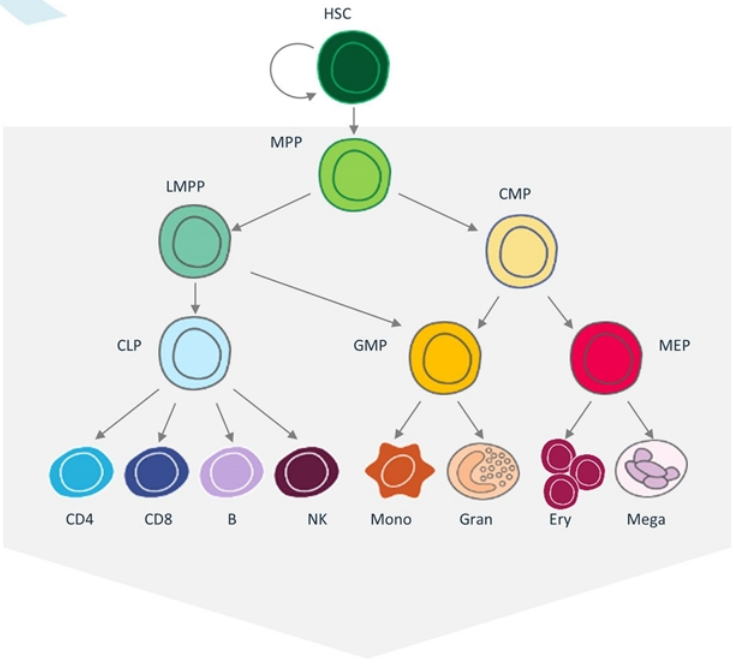
Yeast

Transplant Conditioning

Great need for safer, more specific bone marrow conditioning regimens

Hematopoietic stem cell

Hematopoietic Stem Cell (HSC) Transplants: The Potential to Cure

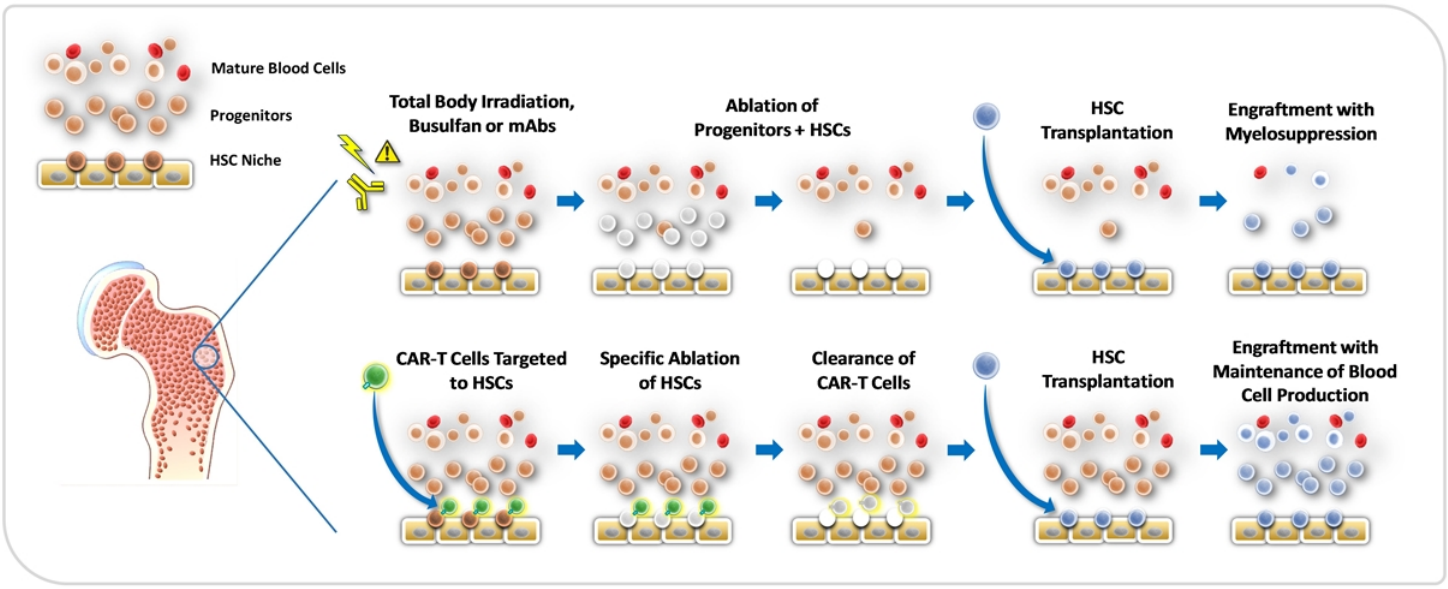


Hematopoietic stem cell transplant (HSCT) renews and re-primes the entire immune system

Risks associated with the procedure generally preclude its use except in cases of fatal disease or high unmet medical need (e.g., oncology)

A safer, more specific conditioning regimen could improve patient outcomes and greatly expand the number of indications (e.g., treatment of autoimmune diseases)

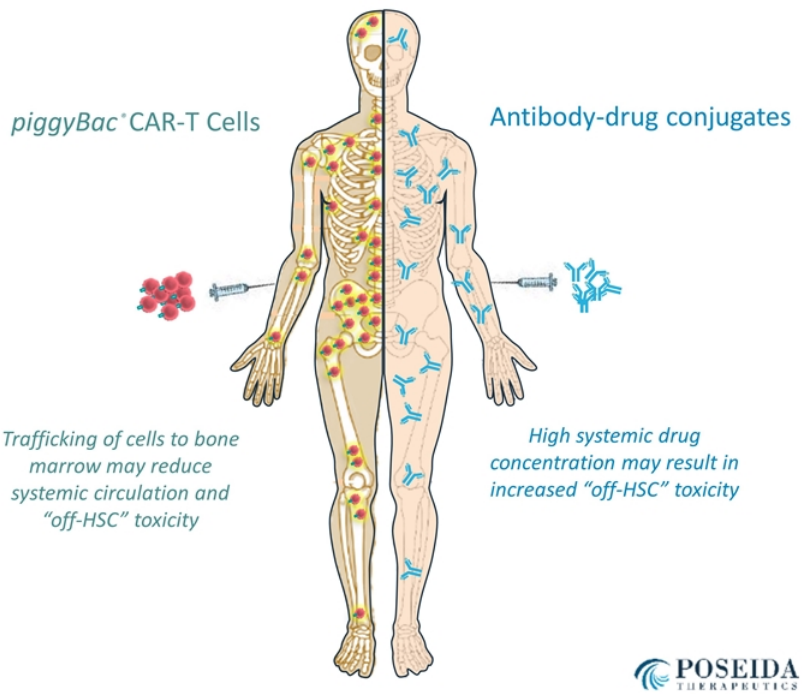
The Concept: CAR-T Cells for Selective Depletion of HSCs Prior to Hematopoietic Stem Cell Transplant (HSCT)



Competitive Advantage of Stem Cell-Directed *piggyBac*® CAR-T Cells

1 **Bone Marrow Homing**

CAR-T cells home and preferentially expand at the site of target cells



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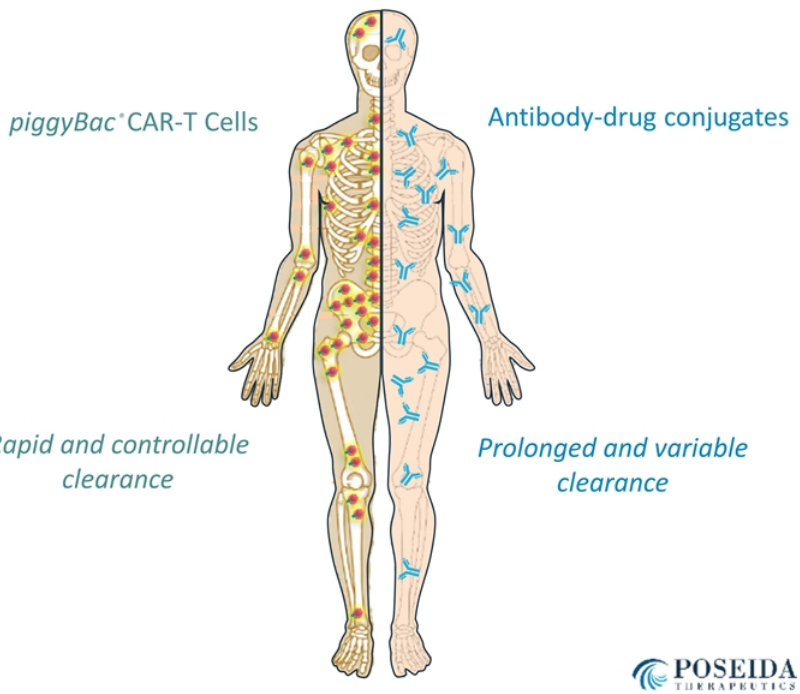
Competitive Advantage of Stem Cell-Directed *piggyBac*® CAR-T Cells

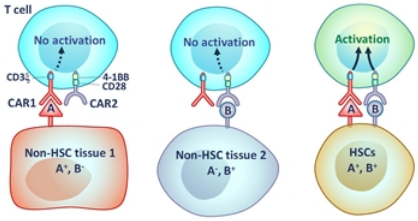
1. **Bone Marrow Homing** — CAR-T cells home and preferentially expand at the site of target cells
2. **Safety Switch** — Rapid clearance of CAR-T cells prior to donor transplant



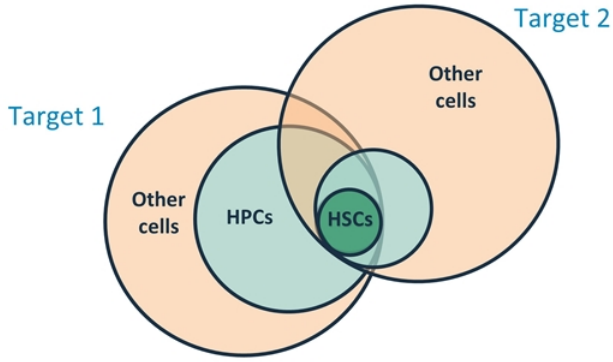
POSEIDA THERAPEUTICS

Competitive Advantage of Stem Cell-Directed *piggyBac*® CAR-T Cells

1. **Bone Marrow Homing** — CAR-T cells home and preferentially expand at the site of target cells
2. **Safety Switch** — Rapid clearance of CAR-T cells prior to donor transplant
3. **Partial Activator CAR** — Potential for highly specific targeting of HSC subset



Combinatorial Dual CAR-T may allow further reduction in off-HSC toxicity

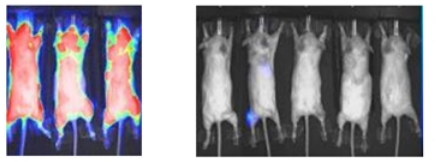


POSEIDA THERAPEUTICS

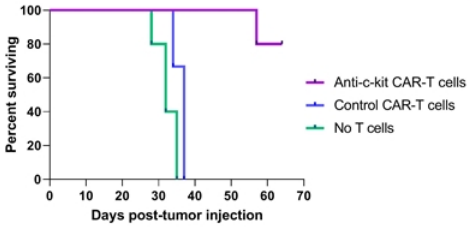
Competitive Advantage of Stem Cell-Directed *piggyBac*® CAR-T Cells

1 Bone Marrow Homing	CAR-T cells home and preferentially expand at the site of target cells
2 Safety Switch	Rapid clearance of CAR-T cells prior to donor transplant
3 Partial Activator CAR	Potential for highly specific targeting of HSC subset
4 Application to Oncology Indications	Lead anti-HSC target doubles as potential AML target

Whole body flux at 28 days post-tumor injection



Overall Survival



Anti-c-kit CAR-T cells clear disseminated disease and significantly prolong survival in the Nomo-1 xenograft model of AML

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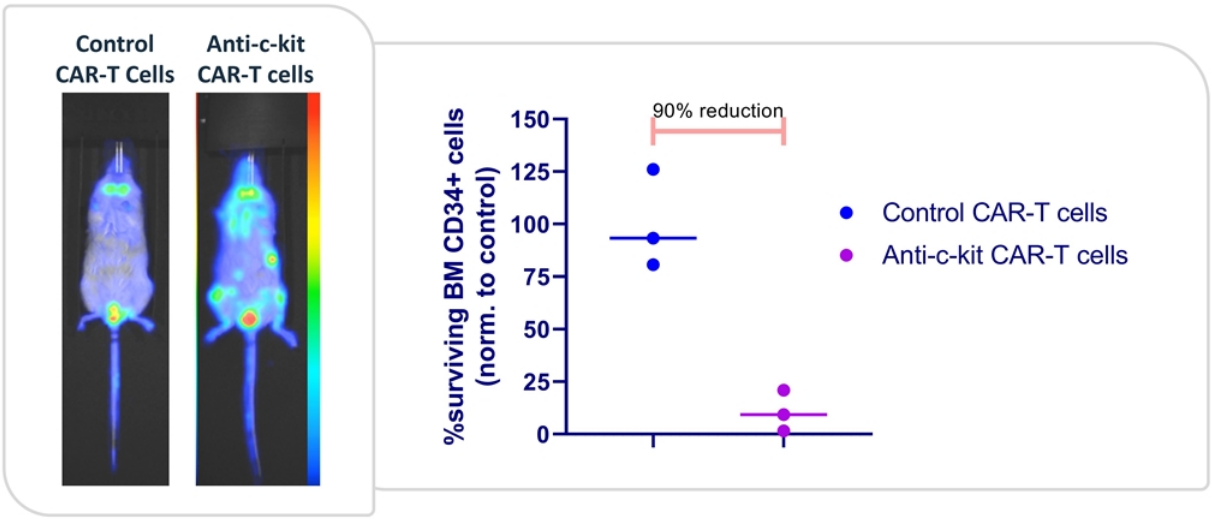
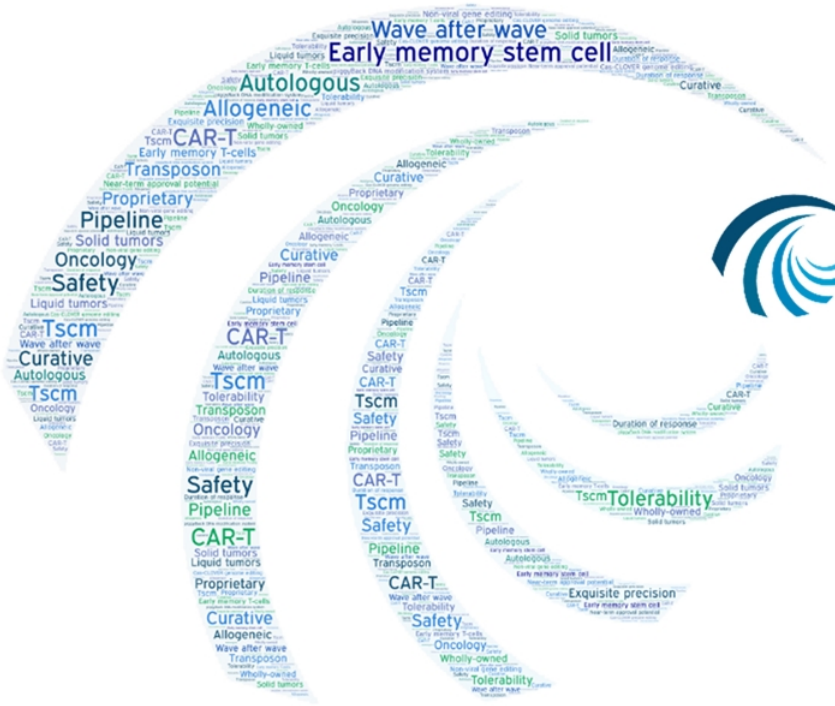
Anti-c-kit CAR-T Cells Accumulate in Bone Marrow and Deplete HSCs



Luciferase labelled CAR-T cells traffic to the bone marrow of humanized mice where they proliferate and kill human CD34+ stem and progenitor cells with 90% depletion measured 10 days post-transplant

Summary

- Safer non-genotoxic conditioning regimens may reduce transplant morbidity and mortality, resulting in better outcomes and a greatly expanded number of potential indications
- Preliminary in vivo experiments have demonstrated the ability of anti-c-Kit CAR-T cells to deplete human stem cell grafts in NSG mice and to prolong survival in a mouse model of AML
- On-going studies will evaluate the use of anti-c-kit CAR-T cells as conditioning agents in a full allogeneic transplant model
- Future progress on this program will intersect with our dual CAR-T and CAR-HSC programs and inform the development of an AML therapy



POSEIDA THERAPEUTICS

Poseida's Ex Vivo Genetic Engineering Platform: Hematopoietic Stem Cells (HSCs)

Claire S. Koechlein, Ph.D.
Associate Director, Research

Translating Our CAR-T Success to Other Cell Types

GENETIC ENGINEERING

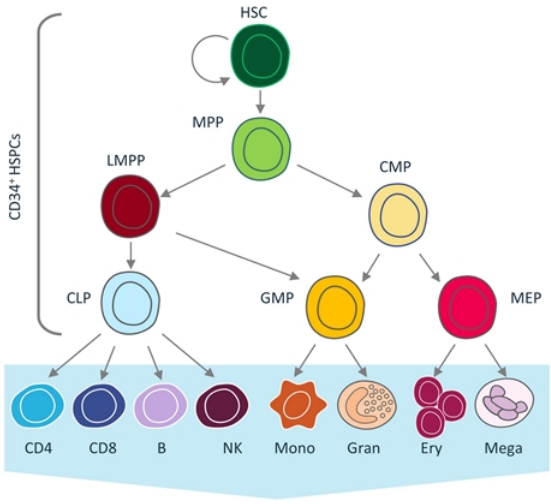
High and durable expression in HSCs via piggyBac® delivery. Efficient KO using Cas-CLOVER™

ADDITIONAL TOOLS

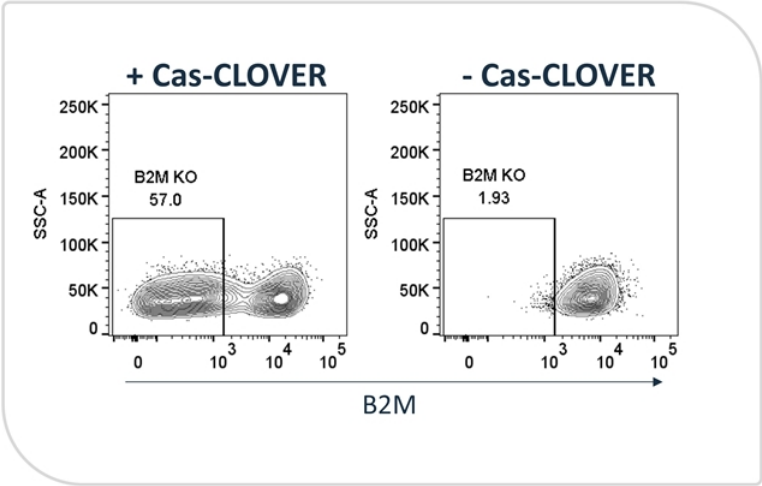
Some tools developed for the T cell programs can be utilized for HSCs (e.g., safety switch, positive selection)

APPLICATIONS

Can create unlimited number of genetically-modified version of any downstream cell type

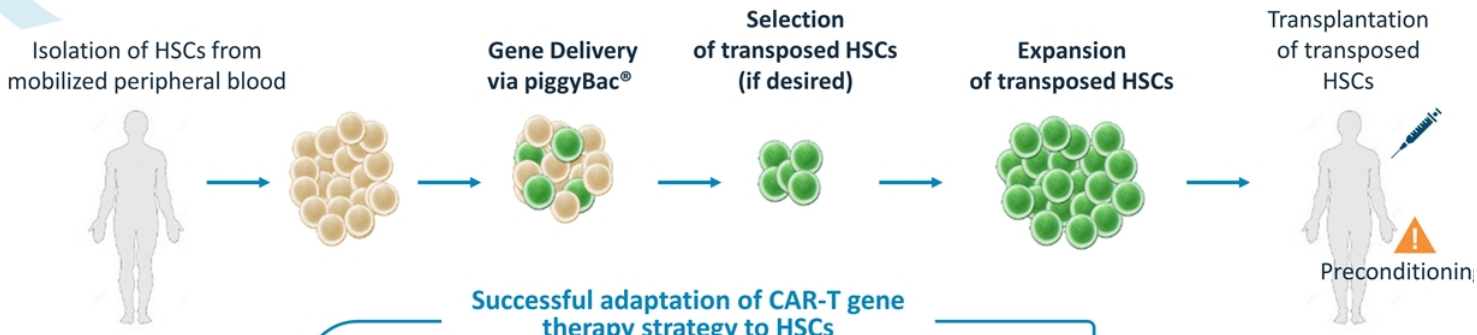


Cas-CLOVER™ Editing is Highly Efficient in HSCs

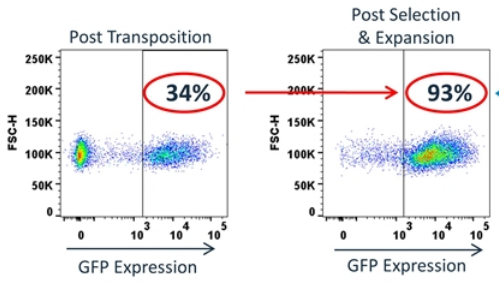


57% Knockout of B2M in achieved in HSCs

Model for piggyBac® Gene Delivery in Hematopoietic Stem Cells



Successful adaptation of CAR-T gene therapy strategy to HSCs



Nearly 100% pure population of genetically modified HSCs after selection

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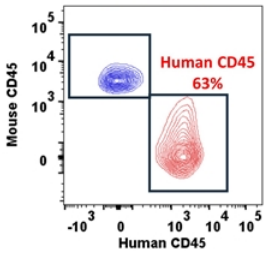
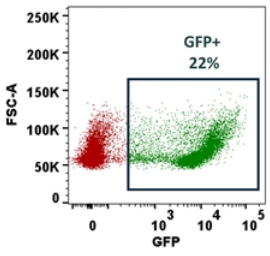
piggyBac® Transposed HSCs can Engraft and Persist In Vivo

Modified HSCs demonstrate robust engraftment in immunodeficient mice

Human Cell Engraftment in Bone Marrow



Transposed Cell Engraftment in Humanized Bone Marrow



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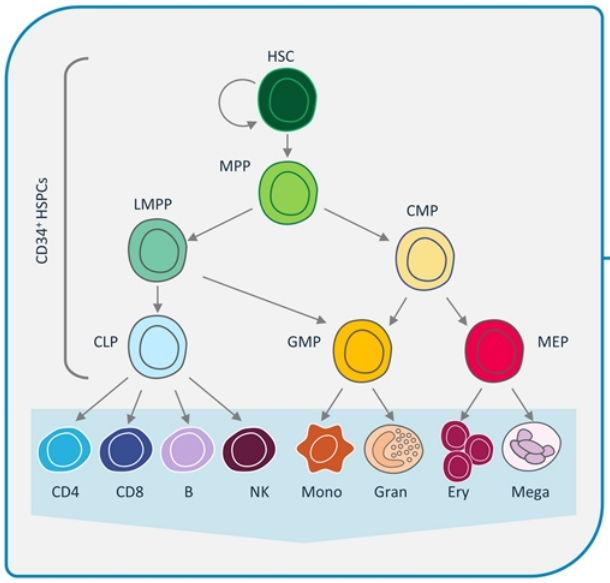
Applications for Our piggyBac® Modified HSC Platform



Disease Indications

- **Genetic Blood Disorders**
  - Examples: Beta-thalassemia, Sickle Cell Disease, Hemophilia A/B, X-SCID
- **Oncology**

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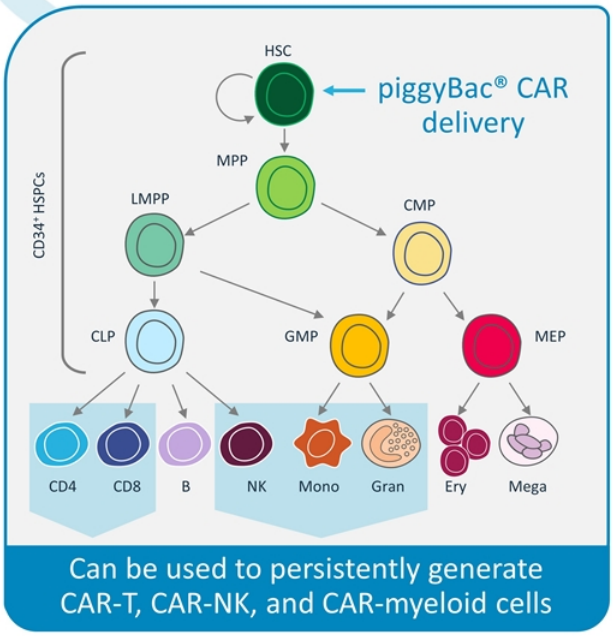
CAR-HSCs Enable the Weaponization of T, NK and Myeloid cells



Can be used to persistently generate CAR-T, CAR-NK, and CAR-myeloid cells

1 Unlimited T_{SCM} CAR-T	piggyBac® CAR gene delivery to a small fraction of transplanted HSCs could provide an inexhaustible supply of T_{SCM} CAR-T cells for continued eradication of recurring malignant cells
2 Diverse CAR Effector Cells	CAR gene delivery to the HSC makes CAR targeting possible in any hematopoietic cell type, including T cells, NK cells, and macrophages
3 Immune Tolerance	Central immune tolerance prevents rejection of CAR-T cells (both humoral and cytotoxic)
4 Safety switch	Proprietary safety switch offers the option for controlled elimination of modified cells post-transplant, if desired

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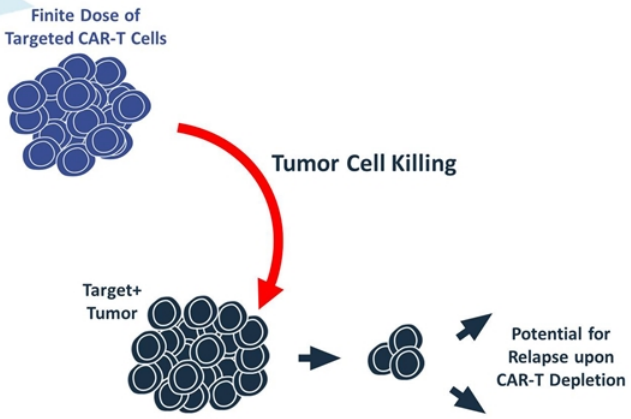
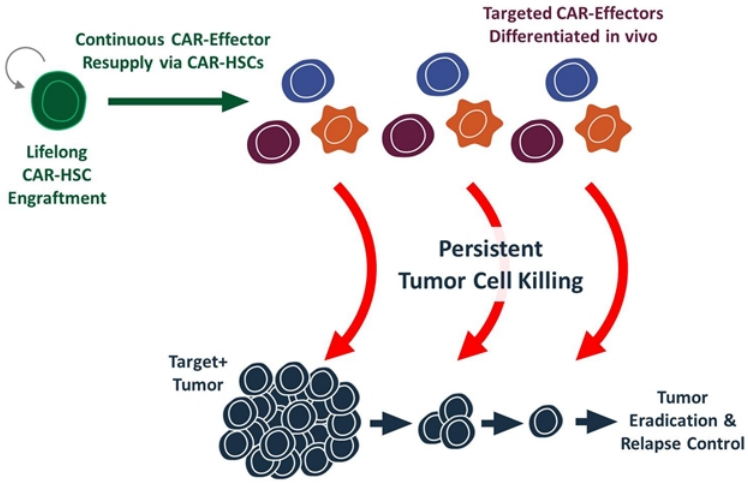
Conventional CAR-T Versus CAR-HSC



CAR-T

Targeted killing limited to the persistence of transplanted CAR-T cells in vivo



CAR-HSC

Lifelong regeneration of targeted CAR effector cells in vivo

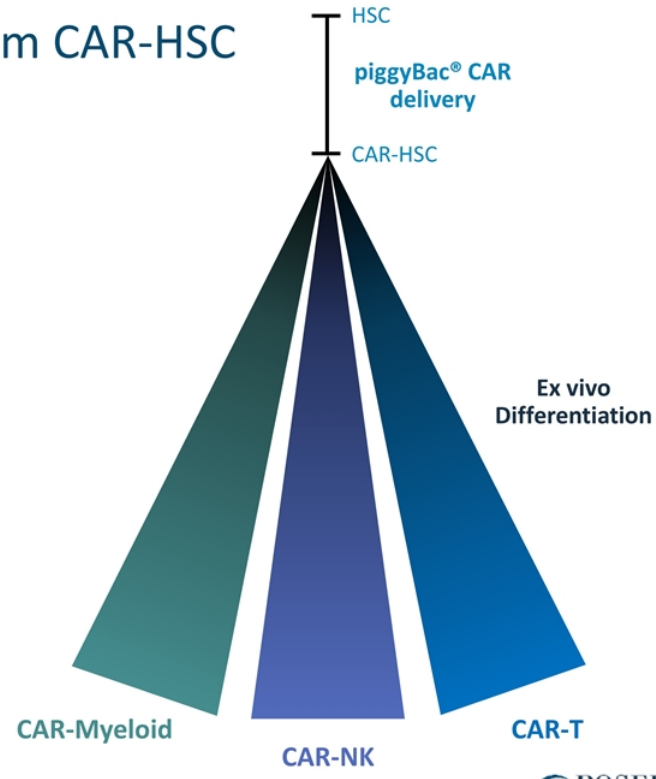
Bioreactor Expansion of Effectors from CAR-HSC

CONCEPT

Ex vivo differentiation of CAR-HSCs into desired effector cells: CAR-T, CAR-NK, CAR-Myeloid

ADVANTAGES

- Utilization of established HSC piggyBac® Gene Delivery System
- Gene delivery to smaller number of cells (input HSCs) lowers reagent and cost demands
- Dramatic cellular expansion ex vivo eliminates dosing limitations of differentiated cells



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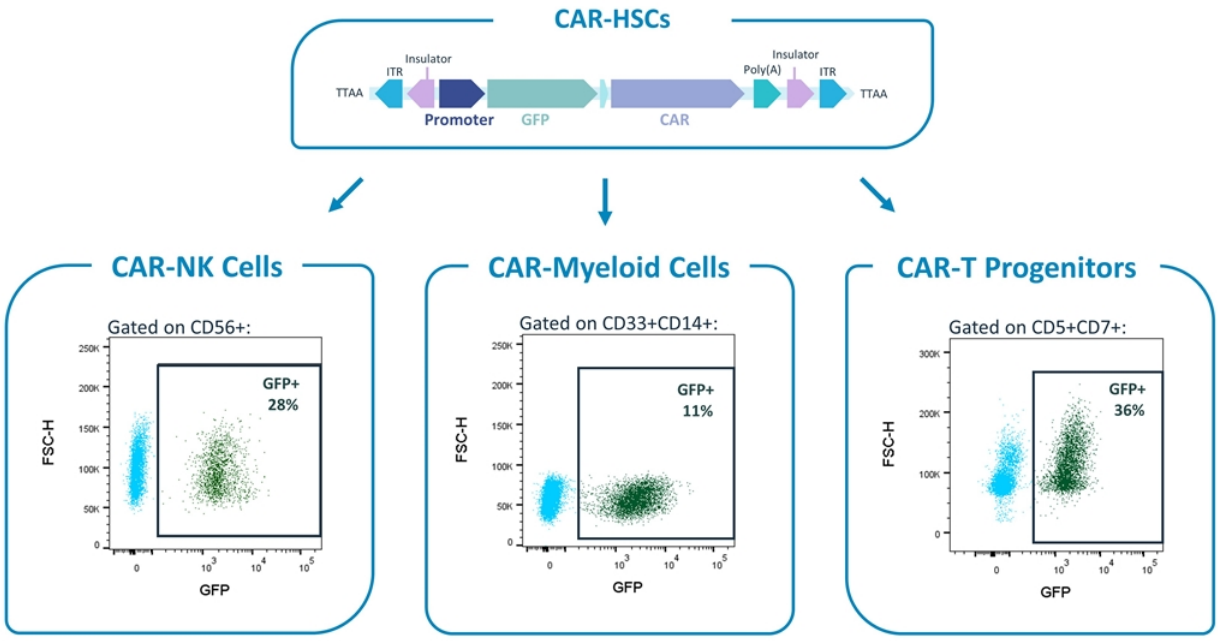
CAR-HSC Differentiated Cells Retain Transgene Expression



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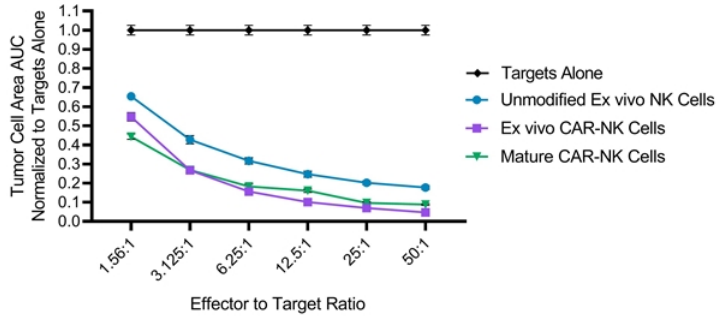
Ex vivo Differentiated CAR-NK Cells are Functionally Comparable to Mature CAR-NK Cells

Cytotoxicity of ex vivo differentiated CAR-NKs



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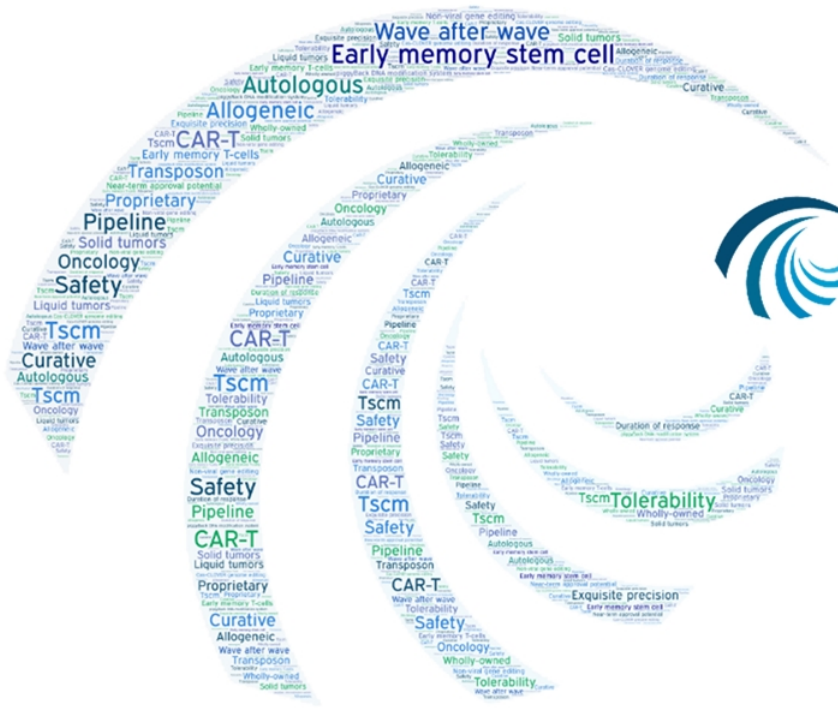
Summary

- HSCs can be modified via the piggyBac® Gene Delivery System and/or the Cas-CLOVER™ Site-Specific Gene Editing System. Genetically modified HSCs engraft in the bone marrow and demonstrate long-term persistence.
- CAR-HSC could be the considered the “ultimate T_{SCM} CAR-T approach” as it provides an inexhaustible supply of effector cells to eradicate tumor.
- CAR-HSCs can be differentiated in an ex vivo ‘bioreactor’ approach to generate high yields of CAR-T, CAR-NK and CAR-Myeloid cells.



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Poseida's Ex Vivo Genetic Engineering Platform: Pluripotent Stem Cells (iPSC/hPSC)

Renata Martin, Ph.D.
Research Scientist,
Genetic Engineering

Gene-Edited iPSCs and their Potential for Regenerative Medicine

POTENTIAL of PLURIPOTENCY

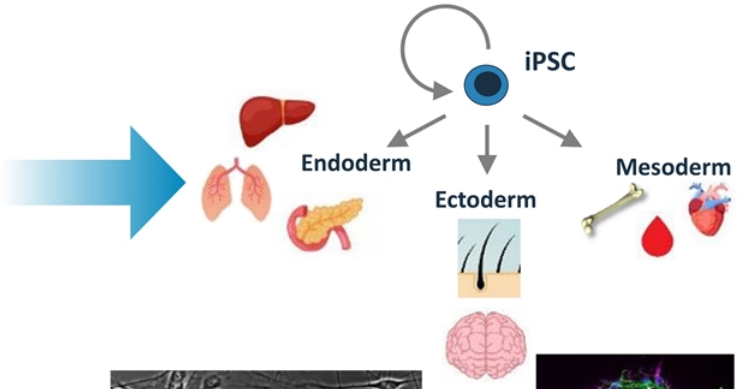
iPSCs can be differentiated into many different cell types (T cells, HSCs, NK cells, Hepatic Progenitors)

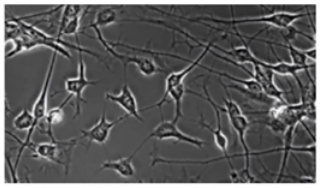
POWER of iPSCs

Can be frozen, thawed, and expanded multiple times without affecting karyotype, enabling endless supplies

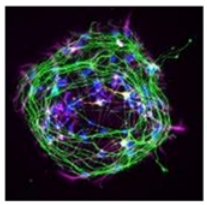
GENE EDITING in iPSCs

Can create successive gene edits, all in a single clone, from which billions of identical cells can be generated





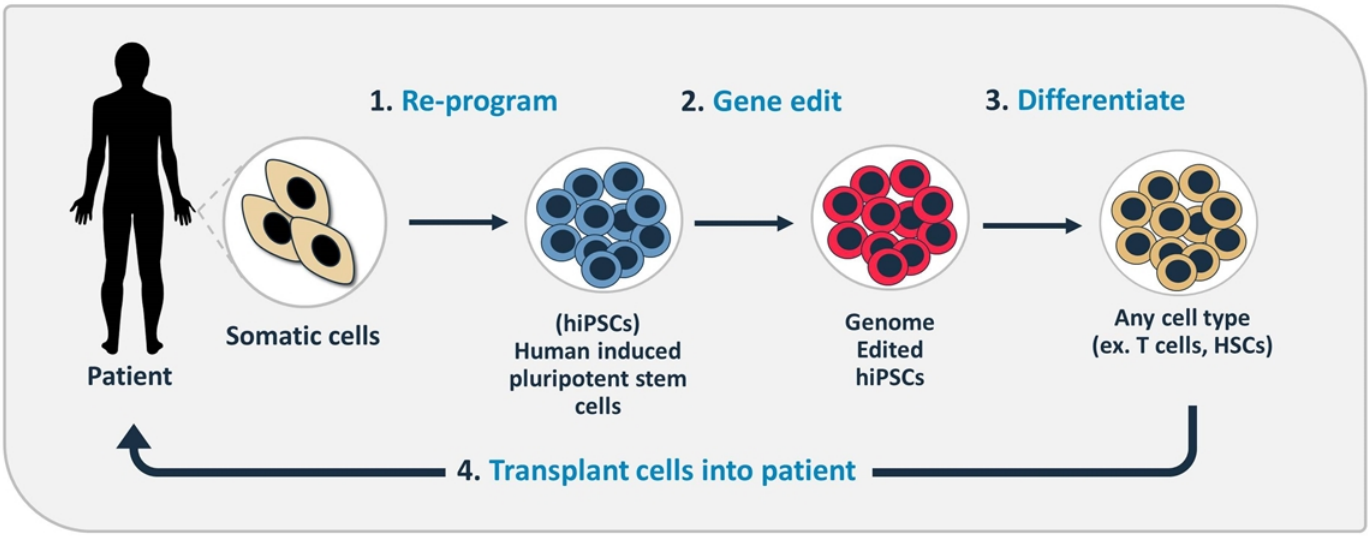
iPSC induced-Neurons



iPSC-derived neuronal circuit

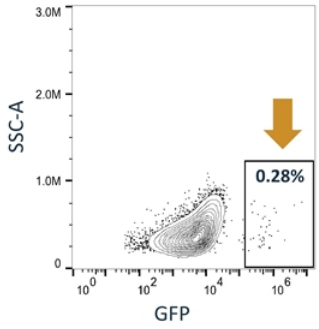
Images from George Church Lab

Combining Cas-CLOVER and iPSC Technology for Therapies



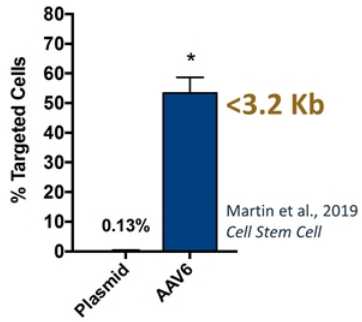
Gene Editing in iPSCs Remains Challenging, Even with CRISPR

Plasmid DNA + Cas9 RNP



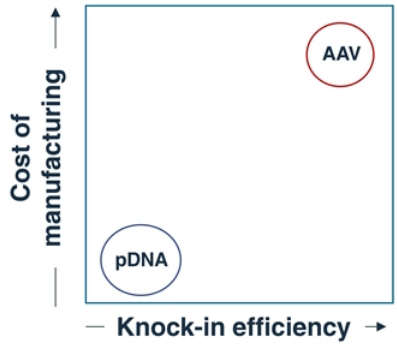
Plasmid Donors Are Inefficient

AAV6/Cas9 editing is efficient



However:
AAV Donors Have Limited Cargo

AAV6-Cas9 is expensive



AAV Knock-ins Yield Variable Efficiency & Have High Costs

CHALLENGE

- **Generate a cost-effective platform for efficient knock-ins of large genes**

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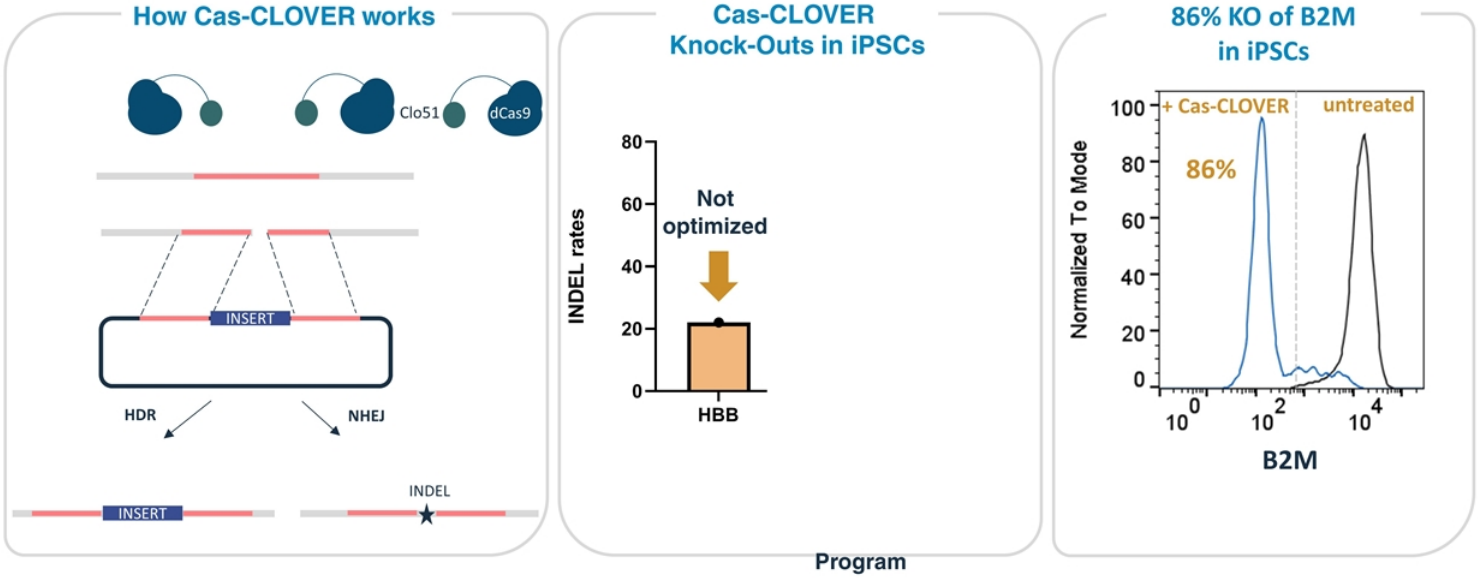
Initial Demonstration of Knock-outs with Cas-CLOVER



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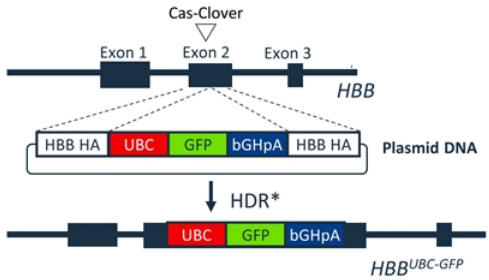
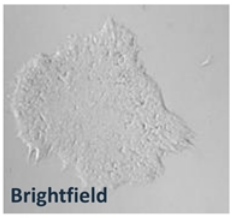
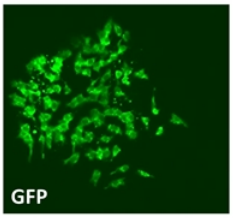
Cas-CLOVER More Efficient Than WT CRISPR for Knock-Ins

Site-specific insertion of a large transgene



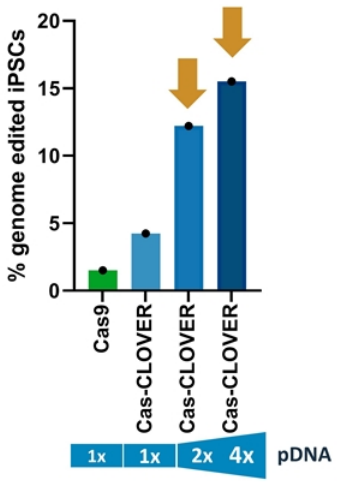




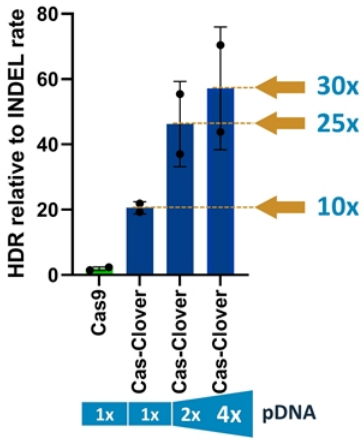
Bulk edited population of iPSCs

*Site-specific insertion confirmed by PCR

More DNA = More Editing



Cas-CLOVER 10-50x More Efficient



Cas-CLOVER vs. WT CRISPR

- ✓ More efficient plasmid-based gene insertion
- ✓ Confers higher tolerance to plasmid DNA
- ✓ Optimization expected to improve further

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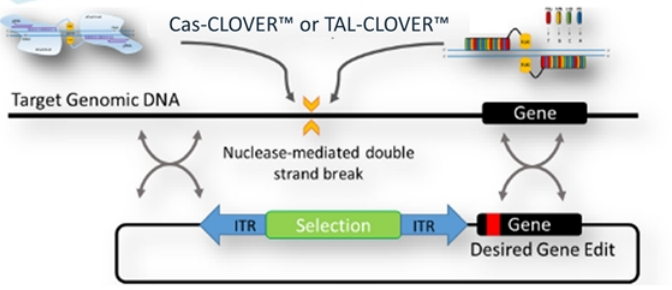
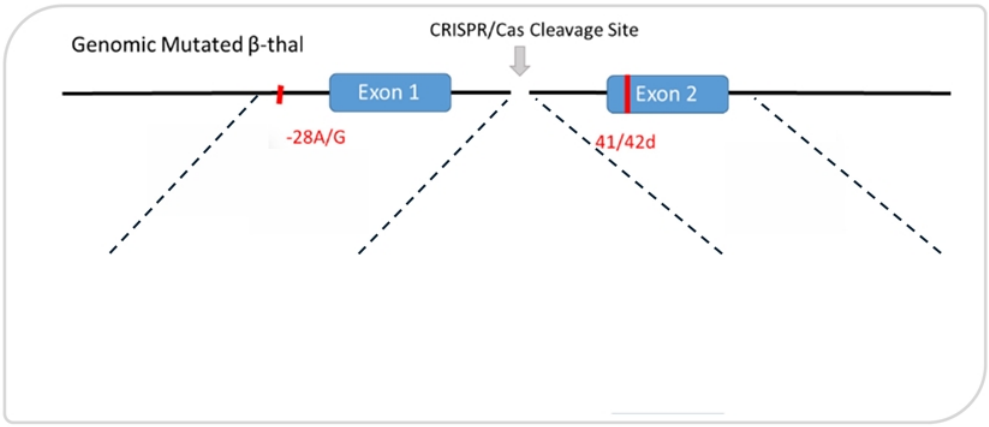
Footprint-Free® Gene Editing



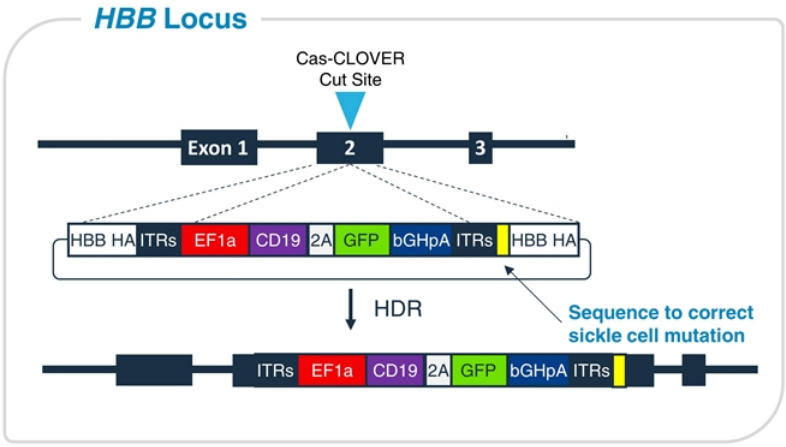
- Combination of Excision-only piggyBac® (PBx) + Cas-CLOVER™ or TAL-CLOVER™
- Ability to select edited cells and then seamlessly remove the selection marker
- Enables one-step cassette removal in both alleles, if necessary
- No unwanted mutations post-excision

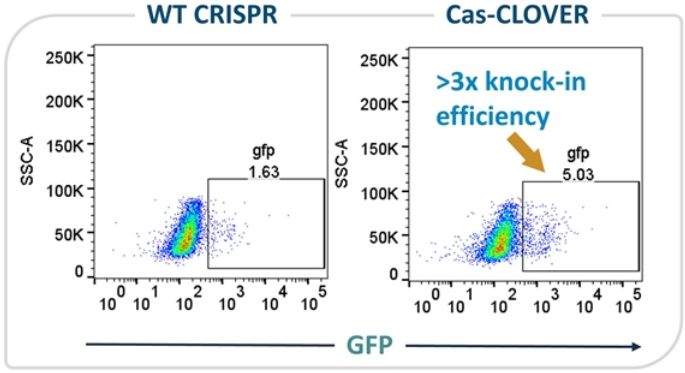
Correction of Genetic Mutations Using Footprint-Free® Gene Editing



Fei Xie et al. (2014) Seamless gene correction of β-thalassemia mutations in patient-specific iPSCs using CRISPR/Cas9 and *piggyBac*. ***Genome Res.***

Cas-CLOVER Facilitates Targeting of a 3.8 kb Footprint-Free™ Cassette





Initial un-optimized conditions yield integration rate 3x better than WT CRISPR

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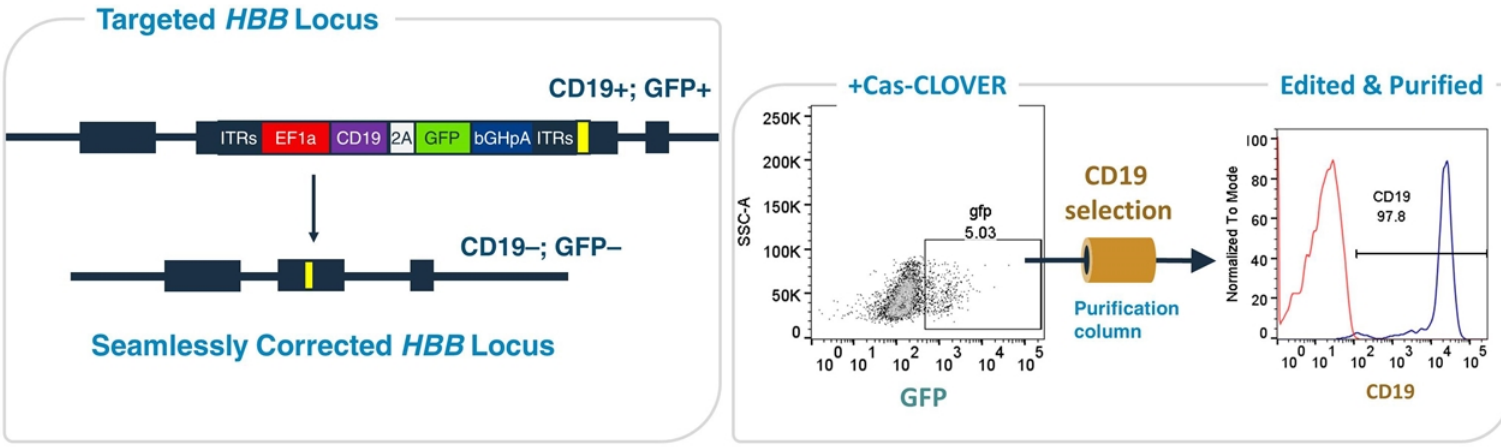
Cas-CLOVER Insertion of HBB Correction & CD19 Purification



1. Positive select (purify) CD19+ cells
2. Remove selection marker with PBx
3. Negative select (remove) CD19+ cells

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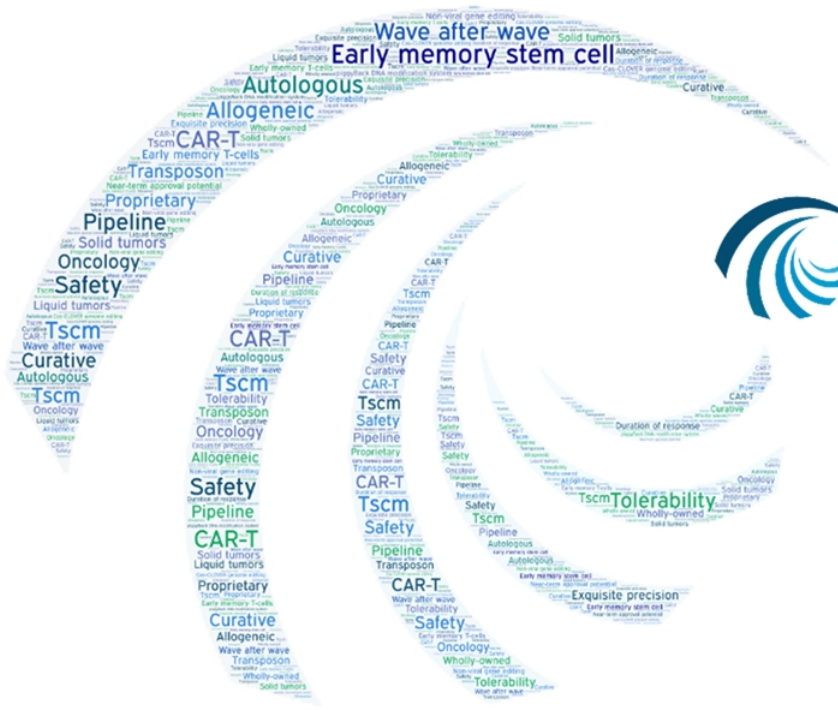
Summary

- Cas-CLOVER is **efficient for knock-outs** in iPSCs, as we observe in T cells and HSCs
- Cas-CLOVER **alleviates toxicity of plasmid DNA**
- Cas-CLOVER **is more efficient than WT CRISPR (Cas9) for knock-ins** using plasmid DNA. Enables therapeutic knock-ins (e.g. correction of sickle cell disease, hemophilia A/B)
- Conditions are currently unoptimized, and with selection/titration of optimal reagents, **efficiencies with Cas-CLOVER are likely to improve substantially**.



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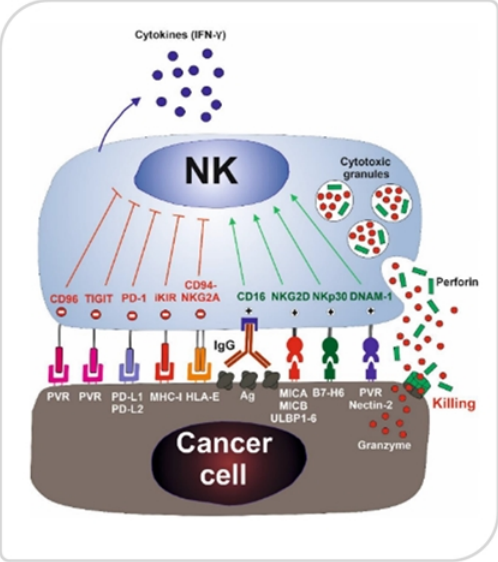
Poseida's CAR-NK Cell Program: Robust production of CAR-NK cells using non-viral piggyBac® system

Stacey Cranert, Ph.D.
Associate Director, Research
Immuno-oncology

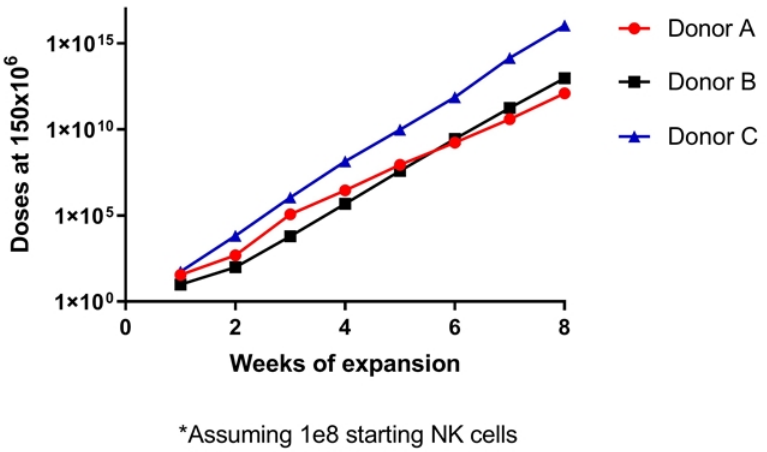
CAR-NK Cells Have Desirable Attributes as a Potential Therapeutic



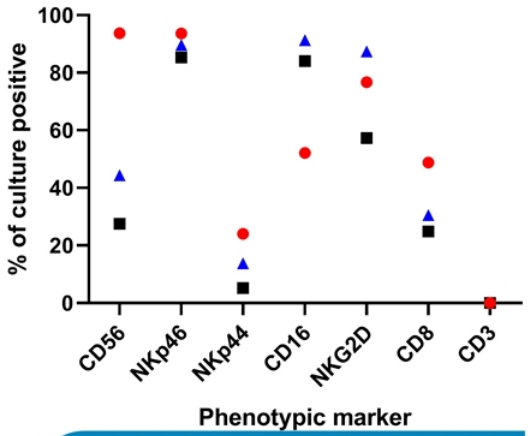
- Natural anti-tumor activity
- Tumor killing can be enhanced with “standard” Chimeric Antigen Receptor (CAR) molecules
- Relatively easy to isolate from healthy donors
- Semi-allogeneic (not TCR-restricted)
- Easy to perform gene knockout with the Cas-CLOVER™ Site-Specific Gene Editing System
- Easy to deliver potentially large transgenes with the piggyBac® Gene Delivery System including armoring mechanisms to enhance NK cell attributes
- Easy to culture to large numbers providing nearly unlimited number of doses at low cost
- Can potentially persist for long periods of time in vivo

J. Clin. Med. **2019**, *8*(10), 1557; https://doi.org/10.3390/jcm8101557

Ex vivo Expansion of NK Cells Yields Extensive Number of Doses

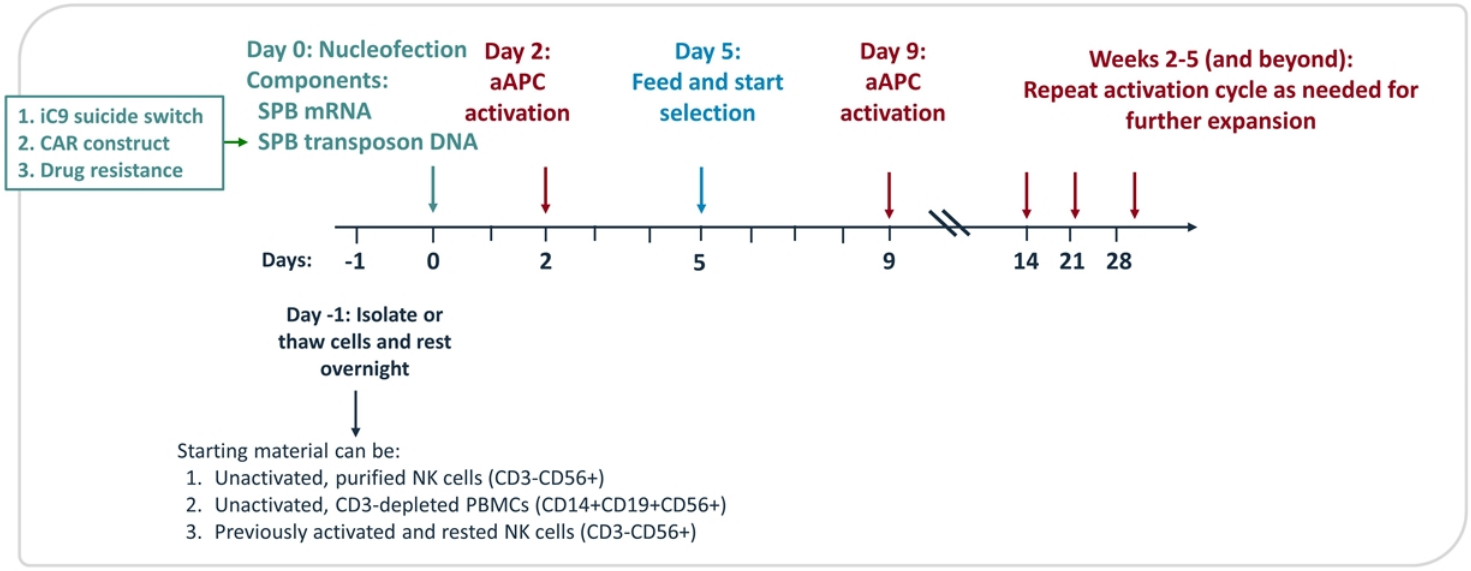


*Assuming 1e8 starting NK cells

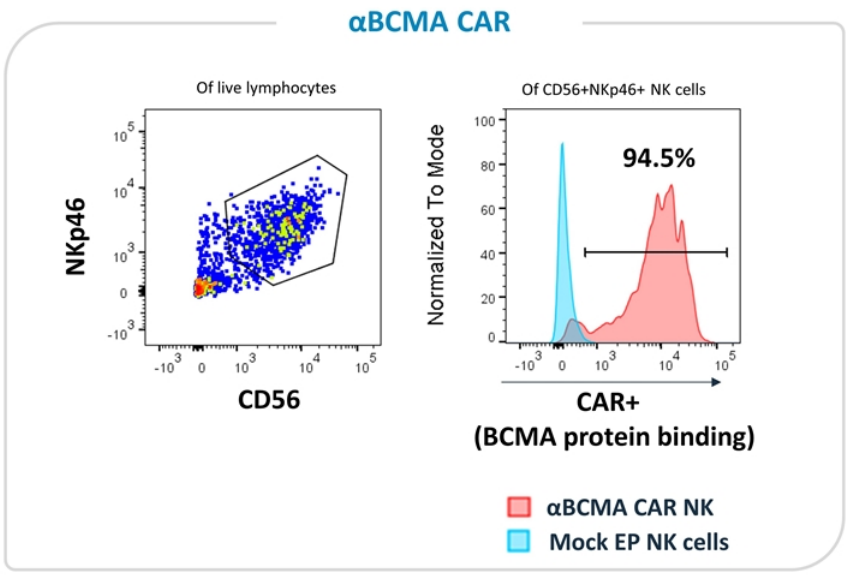


NK cells retain expression profile long term in culture (>25 weeks)

Nonviral piggyBac® Can Be Used to Efficiently Create CAR-NK Cells

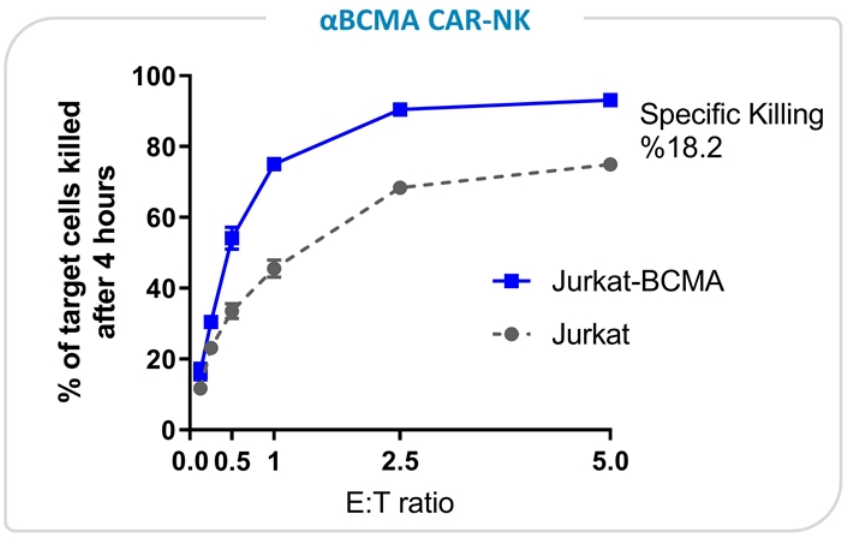


piggyBac® System Generates CAR-NK from Primary NK Cells



- Day 8 post-transposition with piggyBac® CAR construct
- Day 5 post selection with methotrexate (nPB-CAR construct contains DHFR mutein)
- **Final product is 95% CAR-NK cells**

α-BCMA CAR-NK Cells Exhibit Antigen-Specific Cytotoxicity



- 4 hour killing assay
- NK cells maintain cytotoxicity long-term in culture (CAR-NK samples here expanded >2 months)

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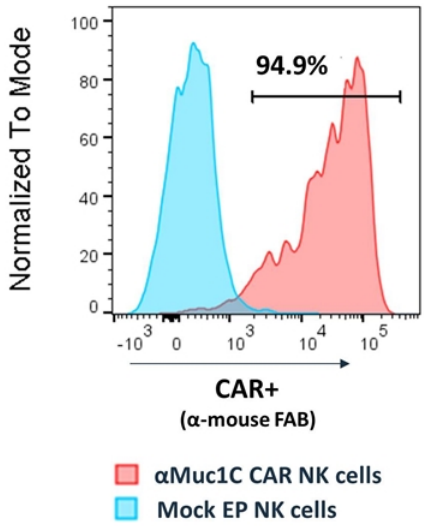
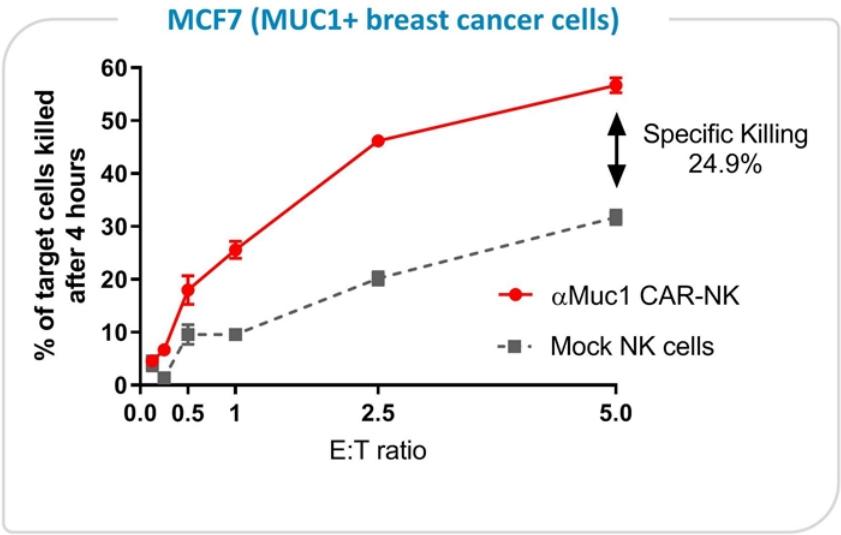
α-MUC1C CAR-NK Cells Exhibit Antigen-Specific Cytotoxicity





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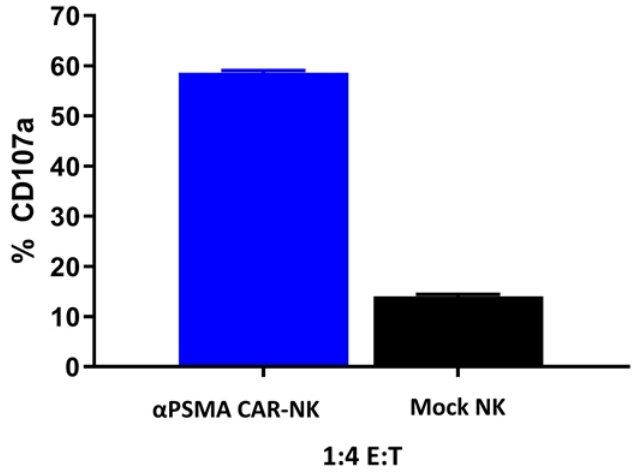
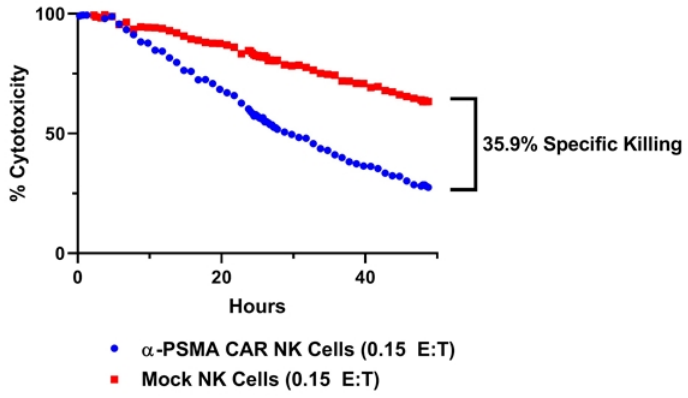
α-PSMA CAR-NK Cells Exhibit Antigen-Specific Cytotoxicity

Degranulation Assay (against PSMA+ LNCaP)



Incucyte Killing Assay (against PSMA+ LNCaP)



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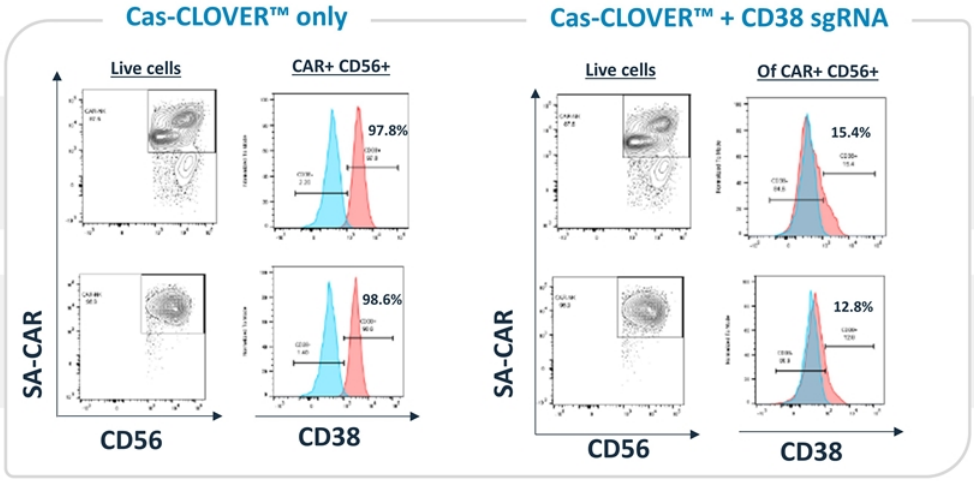
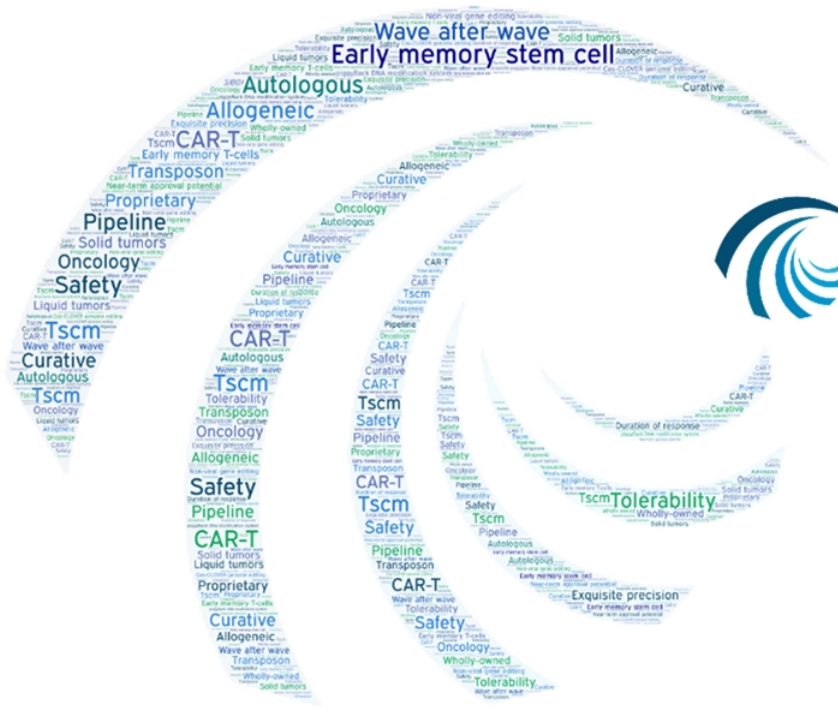
Cas-CLOVER™ Can Be Used to Efficiently Edit piggyBac® CAR-NK Cells



Donor D αBCMA	**82.4% reduction in CD38 expression**
Donor C αMUC1C	**85.8% reduction in CD38 expression**

Summary

- NK cells are a desirable innate lymphoid effector cell for allogeneic cell therapy due to their natural anti-tumor activity, which can be supplemented by non-viral integration of a tumor-specific CAR construct, and their ability to be manufactured in abundance
- The Cas-CLOVER™ Site-Specific Gene Editing System can be used to efficiently edit NK cells or CAR-NK cells
- The piggyBac® Gene Delivery System can be used to effectively deliver large therapeutic transgenes to activated or unactivated peripheral blood NK cells which maintain CAR expression, phenotype and effector function
- The large cargo capacity of the piggyBac® Gene Delivery System allows for inclusion of armoring molecules to improve in vivo persistence, trafficking, and cytotoxicity
- PiggyBac® CAR-NK Cells demonstrate antigen-dependent degranulation and cytotoxicity in vitro against several human cancers



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Conclusion and Closing Remarks

Mark Gergen
President and Chief Business Officer

Poseida's Vision

Developing Transformative Cell and Gene Therapies with the Capacity to Cure

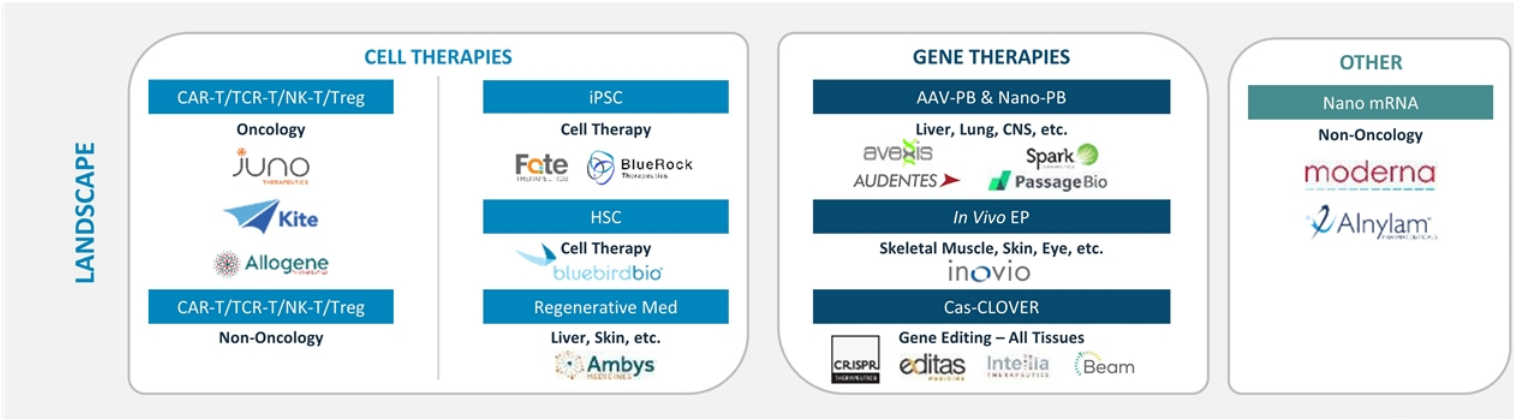
POSEIDA THERAPEUTICS

piggyBac
DNA Modification System

Cas-CLOVER
Gene Editing System

Nanoparticle/AAV
Delivery Technology

Our Broad Next Generation Gene Engineering Platform Technologies are Highly Differentiated and Enable Strategic Opportunities in Many Segments Across Cell and Gene Therapy



We Know We Cannot Develop All Our Technology Alone

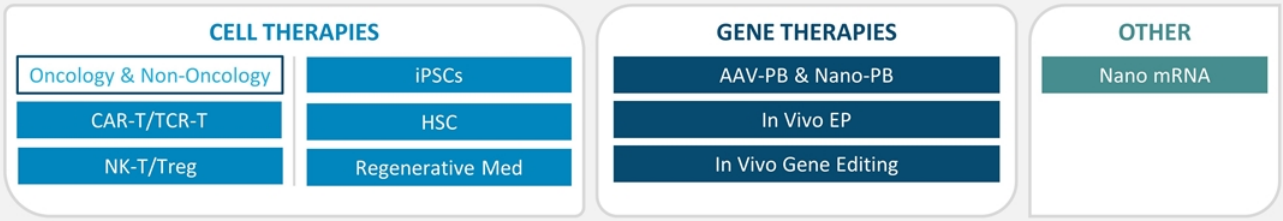
We are Highly Focused on Developing Strategic Relationships To Achieve that Vision

POSEIDA THERAPEUTICS

piggyBac
DNA Modification System

Cas-CLOVER
Gene Editing System

Nanoparticle/AAV
Delivery Technology



- Our technologies are **highly innovative** and represent **a leap forward in cell and gene therapy approaches**
- We are **focused on establishing partnerships and collaborations** to help us drive value creation
- The significant **breadth of our platforms** and pipeline create opportunity for **flexibility in structure**
- **Currently** all platforms and programs are **wholly-owned and unpartnered**

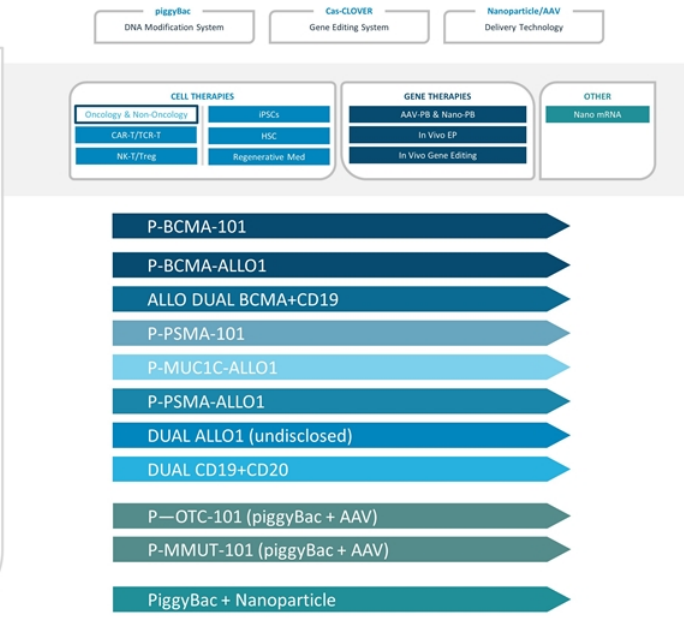
Interested in Collaborating? Connect with us at https://poseida.com/company/partners-collaborators/

Poseida Therapeutics: Investment Hypothesis

Multiple Avenues to Significant Value Creation with Significant Potential Catalysts Ahead

Compelling Investment Hypothesis

- **Innovative and disruptive technology platforms** enable broad **cell and gene therapy** pipeline
- **Multiple milestones and potential catalysts** in next 18 months
- Multiple differentiated **CAR-T** programs in **liquid and solid tumors** including **autologous and a high focus on allogeneic**
- **Novel Gene Therapy** programs address shortcomings of AAV and enabling single treatment cures
- Significant opportunities for **partnership, collaboration and platform expansion**



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Acknowledgements

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Q&A

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