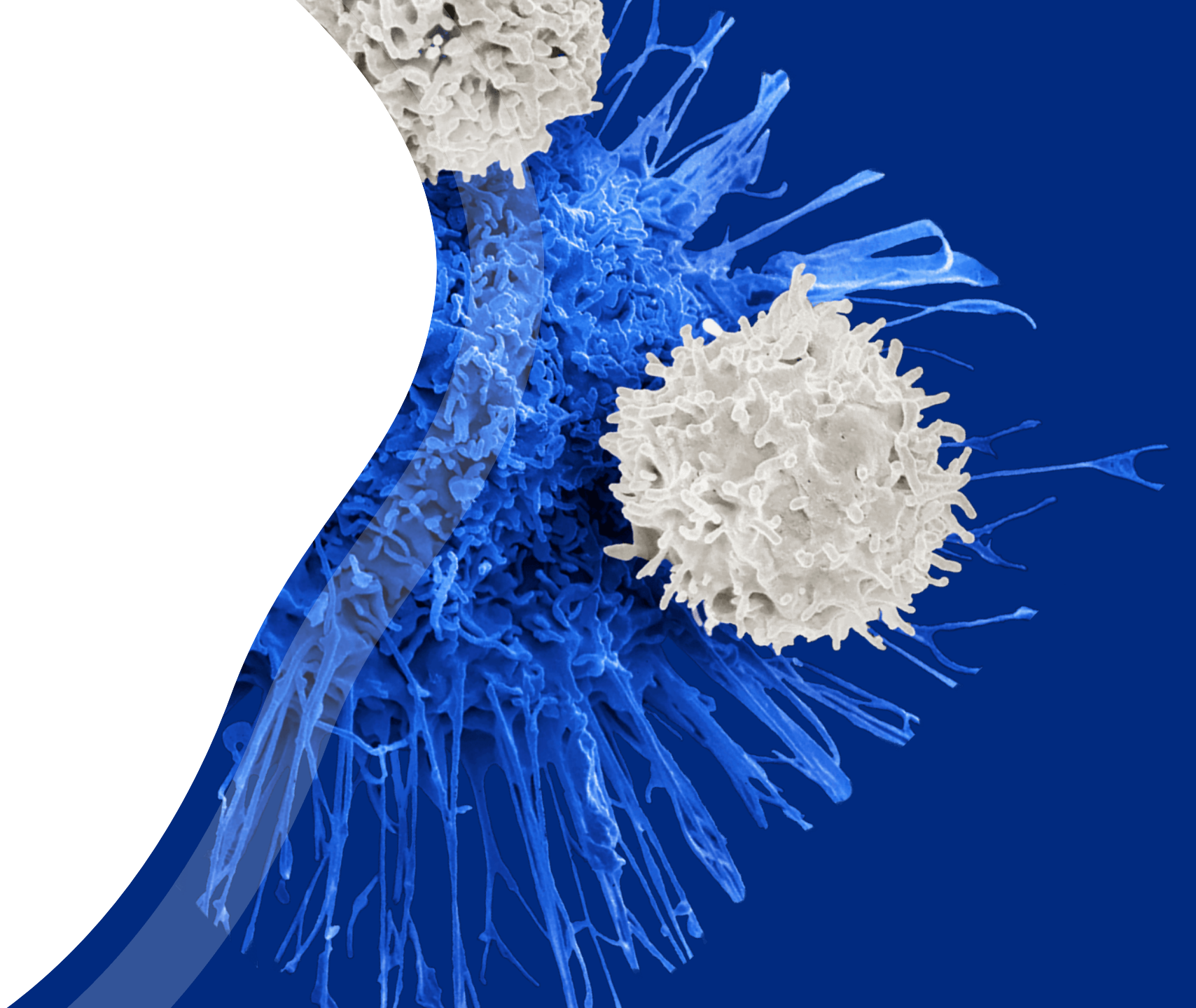
CENTURY THERAPEUTICS

Virtual R&D Day

June 13, 2022



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This presentation contains forward-looking statements within the meaning of, and made pursuant to the safe harbour provisions of, The Private Securities Litigation Reform Act of 1995. All statements contained in this document, other than statements of historical facts or statements that relate to present facts or current conditions, including but not limited to, statements regarding possible or assumed future results of operations, business strategies, research and development plans, regulatory activities, market opportunity, competitive position and potential growth opportunities are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “should,” “expect,” “plan,” “aim,” “seek,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “forecast,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this presentation are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond our control, including, among others: our ability to successfully advance our current and future product candidates through development activities, preclinical studies, and clinical trials; our reliance on the maintenance on certain key collaborative relationships for the manufacturing and development of our product candidates; the timing, scope and likelihood of regulatory filings and approvals, including final regulatory approval of our product candidates; the impact of the COVID-19 pandemic, geopolitical issues and inflation on our business and operations, supply chain and labor force; the performance of third parties in connection with the development of our product candidates, including third parties conducting our future clinical trials as well as third-party suppliers and manufacturers; our ability to successfully commercialize our product candidates and develop sales and marketing capabilities, if our product candidates are approved; and our ability to maintain and successfully enforce adequate intellectual property protection. These and other risks and uncertainties are described more fully in the “Risk Factors” section of our most recent filings with the Securities and Exchange Commission and available at www.sec.gov. You should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Agenda

Building A Next-Generation iPSC Platform

Lalo Flores, PhD, CEO

GBM Landscape and Opportunity

Shelia Singh, MD, PhD, Professor of Surgery and Biochemistry, Chief Pediatric Neurosurgeon at McMaster Children's Hospital, the Division Head of Neurosurgery at Hamilton Health Sciences, and the Inaugural Director of McMaster's New Cancer Research Centre

iNK Cells Provide Enhanced Control in the Treatment of GBM

Hy Levitsky, MD, Head of R&D

Century's iNK 3.0 platform
iNK common progenitor and Next-Gen CNTY-103

Luis Borges, PhD, CSO

Century's Novel Universal Targeting Receptor Adaptor Platform

Jill Carton, PhD, Executive Director of CAR Engineering and Protein Sciences

MAD7 CRISPR Nuclease for iPSC Genome Engineering

Michael Naso, PhD, VP Cell Engineering

Q&A

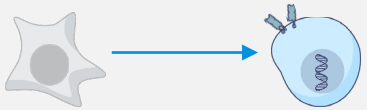
CENTURY
THERAPEUTICS

Building A Next-Generation iPSC Platform

Lalo Flores, PhD I CEO

Building a Next Generation Allogeneic Cell Therapy Platform

iPSC Reprogramming

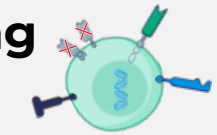


- Comprehensive collection of clinical grade lines (CD34+ HSC, αβ T cell, γδ T cell derived)

Gene Editing

- Proprietary gene editing platform
  - CRISPR MAD7-derived gene editing for precise transgene integration

iPSC Differentiation/Manufacturing



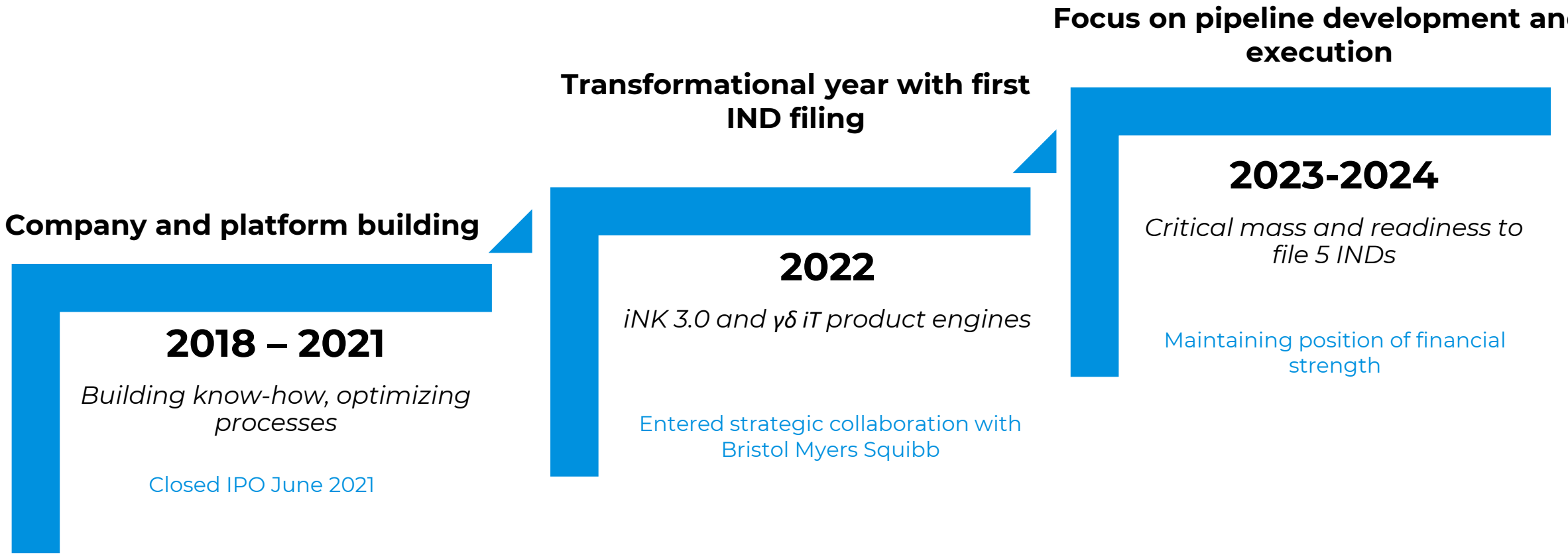
- Scalable protocols and processes to produce highly functional iNK and iT cell products

Protein Engineering

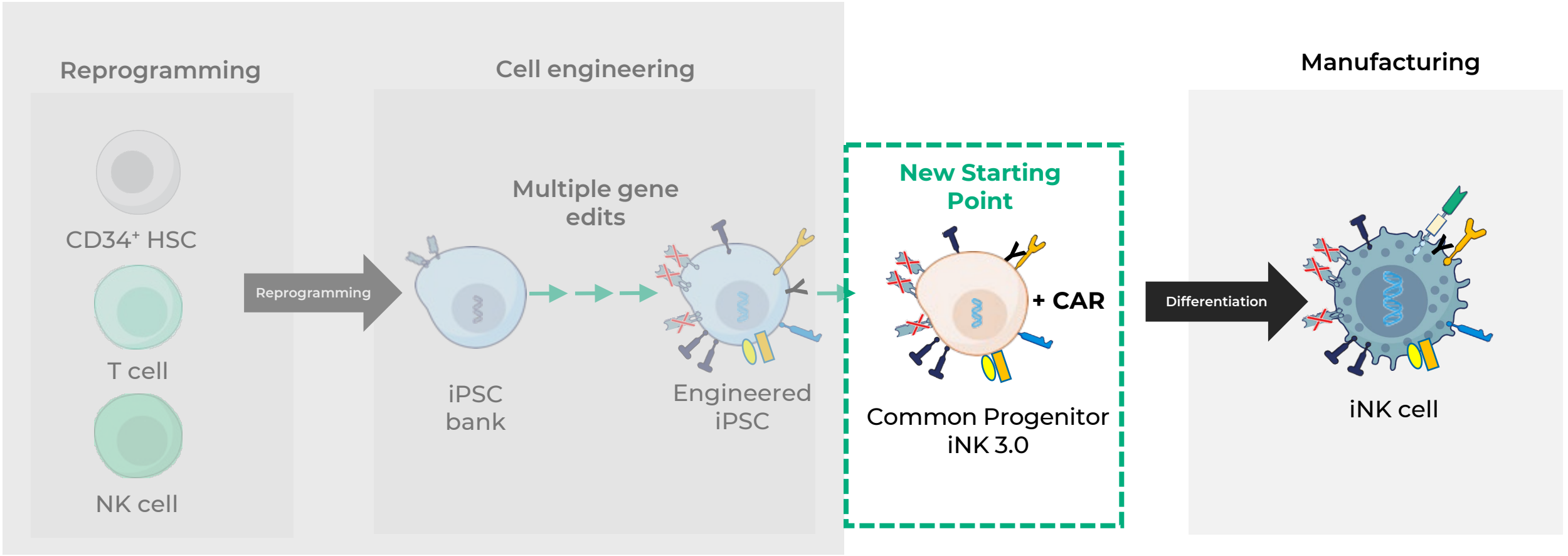
- Developing proprietary next-generation CARs
- Universal tumor targeting platform

Vertically integrated capabilities differentiate Century's approach

With a Strong Foundation in Place, Century is Ready to Execute



Common Progenitor Milestone Enables Cost, Time Efficiencies



- iPSC cell bank with 12 core 3.0 gene edits introduced in 5 sequential steps
- Resets product development starting point: accelerates and de-risks development candidate selection

Pipeline

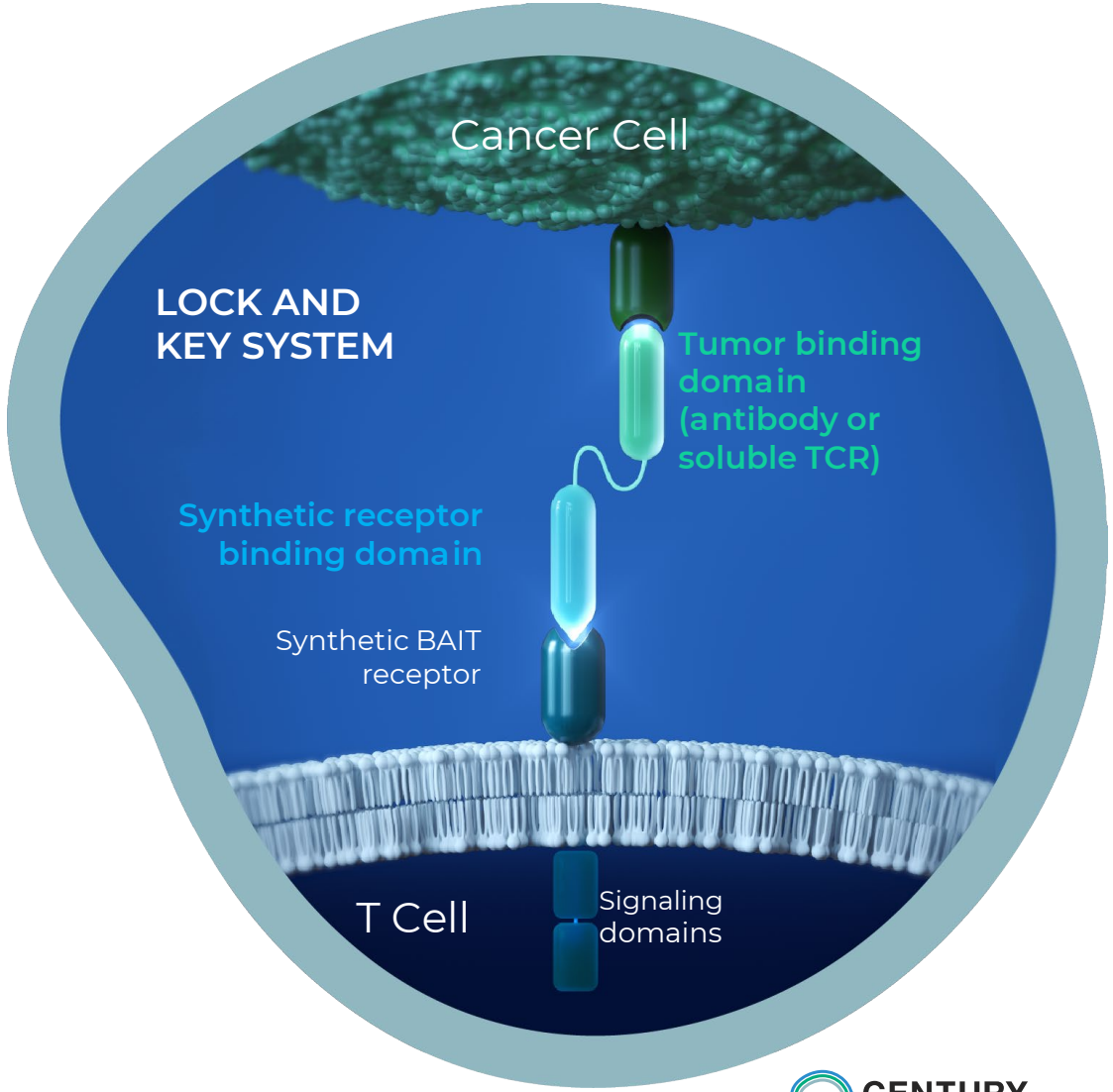
Product candidate pipeline across cell platforms and targets in solid and hematologic cancers

Solid Tumors Hematologic Tumors

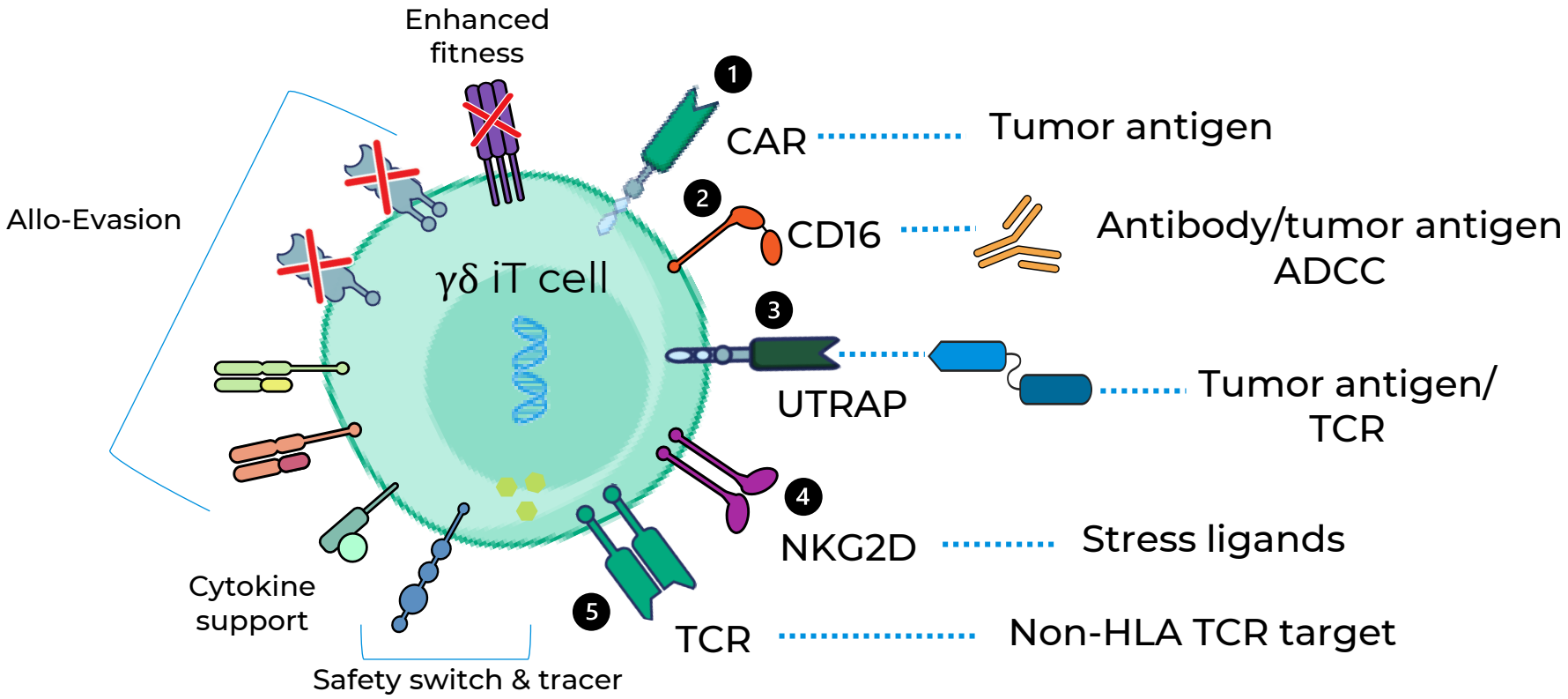
Product	iPSC Platform	Targets	Indications	Expected IND Submission	Discovery	Preclinical	Clinical	Collaborator
CNTY-101	iNK	CD19	B-Cell Malignancies	Mid 2022				
CNTY-103	iNK	CD133	Glioblastoma	2024				
CNTY-102	iT	CD19 + CD79b	B-Cell Malignancies	2024				
CNTY-104	iNK/iT	Multi-specific	Acute Myeloid Leukemia	2024				Bristol Myers Squibb
CNTY-106	iNK/iT	Multi-specific	Multiple Myeloma	2024				Bristol Myers Squibb
Discovery Research Programs								
	iNK/iT	TBD	Solid Tumors	TBD				
	iNK	TBD	Hematological Tumors	2023				

Universal Tumor Antigen Receptor Targeting Platform (uTRAP)

- Multifaceted tumor targeting platform
  - Compatible with soluble CARs and TCRs
  - Potentially enables targeting of multiple TAAs with single cell product
- Selective for allogeneic cell vs CD3-based bispecific antibodies and CD16 NK engagers



Century's Strategic Vision for Winning in Solid Tumors



Building best-in-class γδ iT cell platform with up to 5 distinct tumor killing mechanisms

Anticipated Catalysts Over Next 12 months

Underpinned by strong balance sheet with platform synergies and operational excellence

CNTY-101

Becoming clinical stage biotech company with most advanced allogeneic cell therapy

- IND submission (Mid-2022)
- Phase 1 (ELiPSE-1) start in B-cell malignancies (2H22)

γδ iT Platform

Leveraging the comprehensive end-to-end platform

- γδ iT pre-clinical data (4Q22)

iNK 3.0 Common Progenitor

Creating platform efficiencies

- Select additional candidate based on iNK 3.0 (YE22) – disclose data at future medical meeting
- CNTY-103 development candidate (2023)

Disclosures

5 INDs anticipated over next 3 years

- Solid tumor candidate expected to be announced (4Q22)

AACR American Association for Cancer Research®

ANNUAL MEETING 2022 New Orleans

APRIL 8-13, 2022 • #AACR22

Targeting Clonal Heterogeneity in Treatment-refractory Brain Cancers with Rationally Designed Immunotherapies: Advances and Challenges

AACR Meet-The-Expert Session

April 10th, 2022

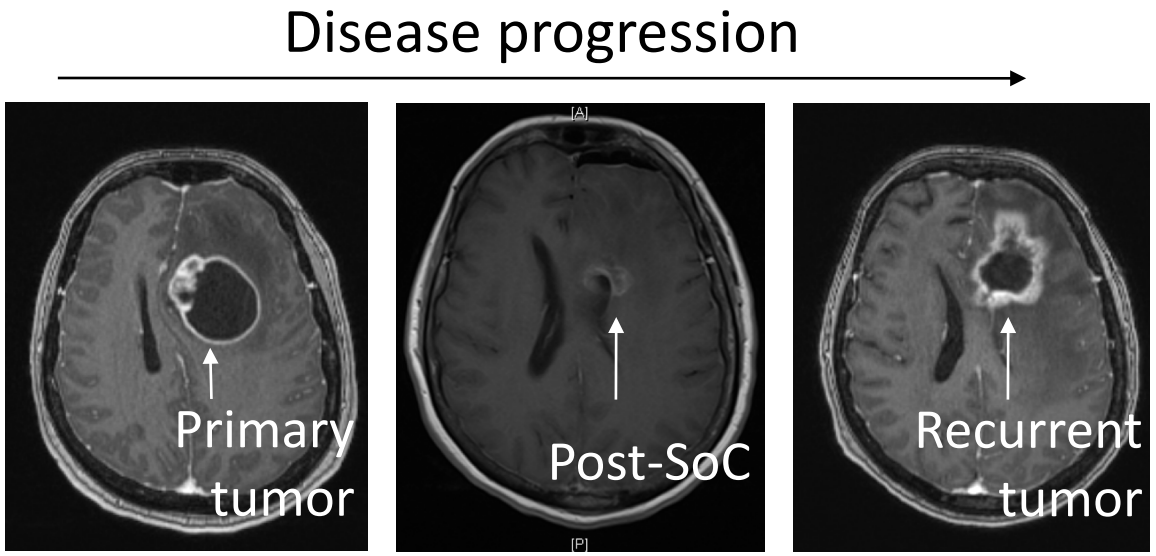
Sheila K. Singh MD PhD FRCS(C)

McMaster University, Hamilton, ON, Canada

McMaster University | BRIGHTER WORLD

Glioblastoma is an aggressive disease

Most prevalent primary brain tumor in adults causing death



Standard of care (SoC):

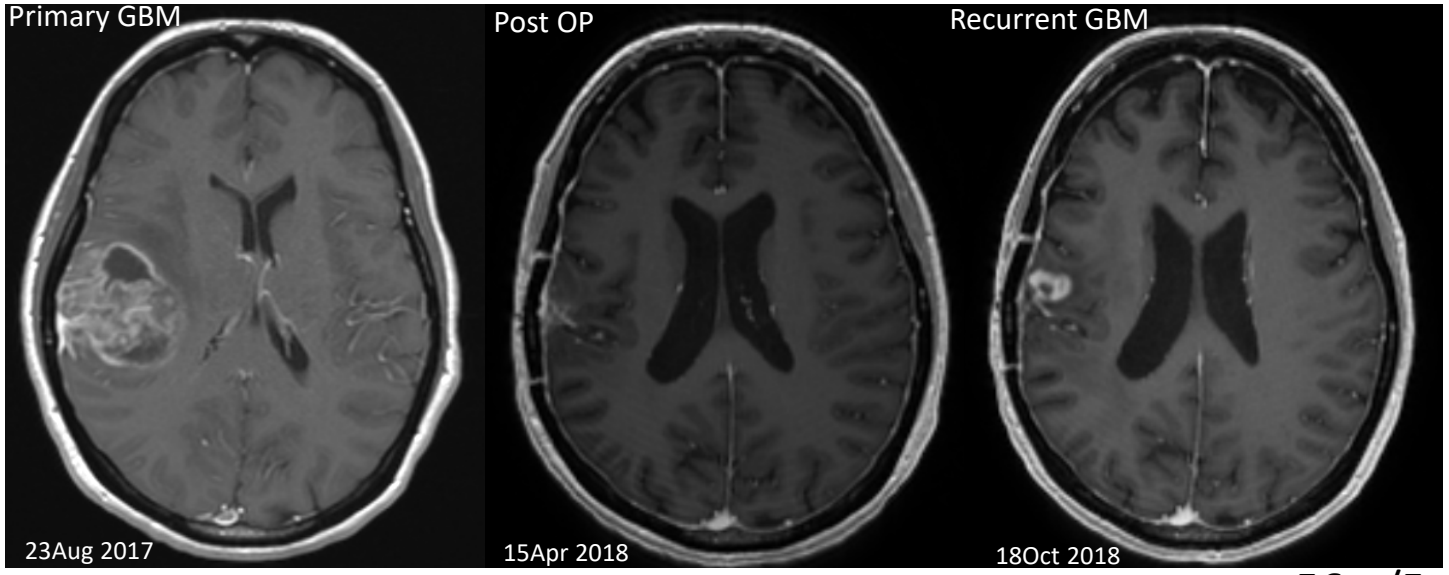
- Surgical resection
- Radiation
- Chemotherapy with Temozolomide

Patients succumb to recurrent disease with a median overall survival of <15-17 months

Glioblastoma (GBM) Overview

FOCUS – Unmet need in brain cancer therapy

- 9-month relapse period
- 15 months median survival post-diagnosis
- ~5% five-year relative survival



56yr/F

COMMERCIAL POTENTIAL

- ~13,390 new cases diagnosed in 2020 in the US[1]
- Global GBM treatment market to reach USD $1.15 billion by 2024[2]
- In 2016, North America contributed 39.2% of the global GBM market[2]
- Opportunity to acquire orphan/breakthrough designation

1. American Brain Tumor Association
2. Hexa Research

GBM Market landscape – Limited competition

A total of 139 drugs currently in clinical development in primary and recurrent GBM

PHASE	SMALL MOLECULES	BIOLOGICS	OTHERS (CAR-Ts, viruses, vaccines, etc
Approved	3 (Temozolomide, carmustine/ carmustine implant)	3 (bevacizumab and 2 biosimilars)	0
Phase III	9	6	8
Phase II	22	11	10
Phase I	41	22	10
Total	72	39	28

- Limited approved treatment options
- Small number of late-stage development
- Early development players largely small companies

12 CAR-T trials: EGFRvIII, BAFFR, IL13R, EphA2, CD133 and HER2

Data from BioMedTracker

Glioblastoma: A Graveyard of Clinical Trials, or Unmet Opportunity?

- First-line standard of care was developed @ 20 years ago.
- SoC is far more effective in MGMT- methylated vs. unmethylated patients but used regardless of biomarker status due to lack of targeted options.
- Second-line options include lomustine or bevacizumab, the latter which provides marginal benefit, causes pseudo-progression, and renders subsequent intervention essentially ineffective.

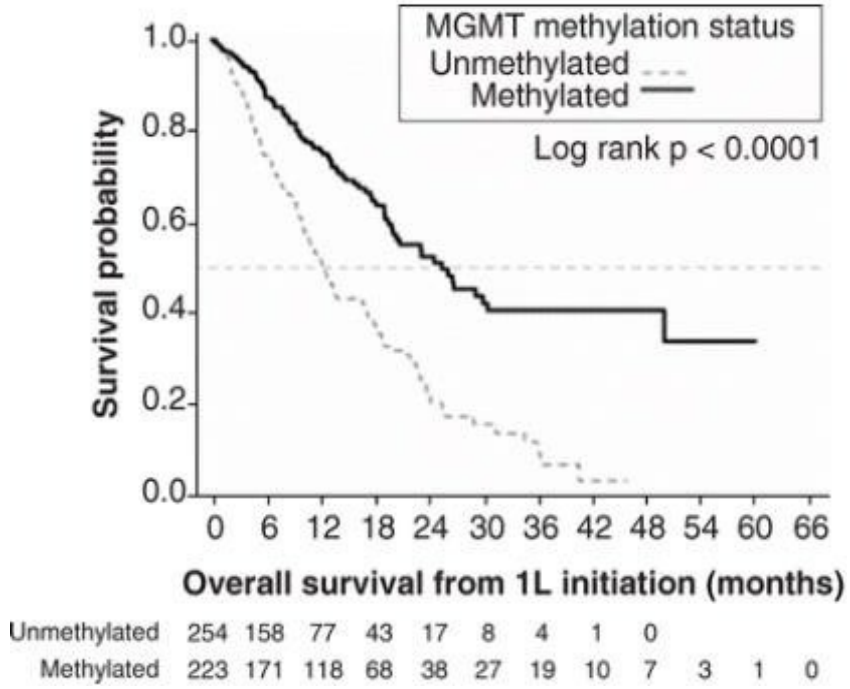
♦ **Historical failures arguably due to solvable problems**

- Companies tend to focus on GBM as a line-extension of programs being developed elsewhere and hence may not be prioritizing as necessary to win in GBM
- Furthermore, many of the therapeutic targets (EGFR, VEGF) are relevant in treatment-naïve patients but become selected against following frontline therapy.

"Every surgeon carries within himself a small cemetery, where from time to time he goes to pray."

- Dr. René Leriche: from epigraph to "Do No Harm,"

Dr. Henry Marsh



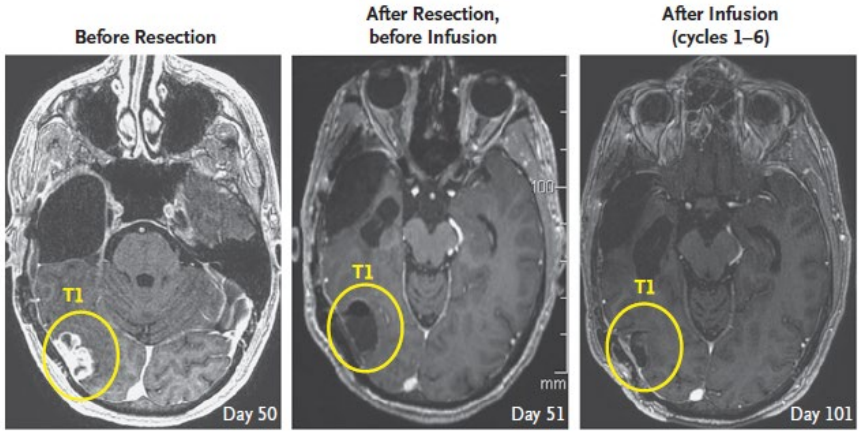
CAR T Cell Therapies for GBM: the Promise of Locoregional Delivery

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

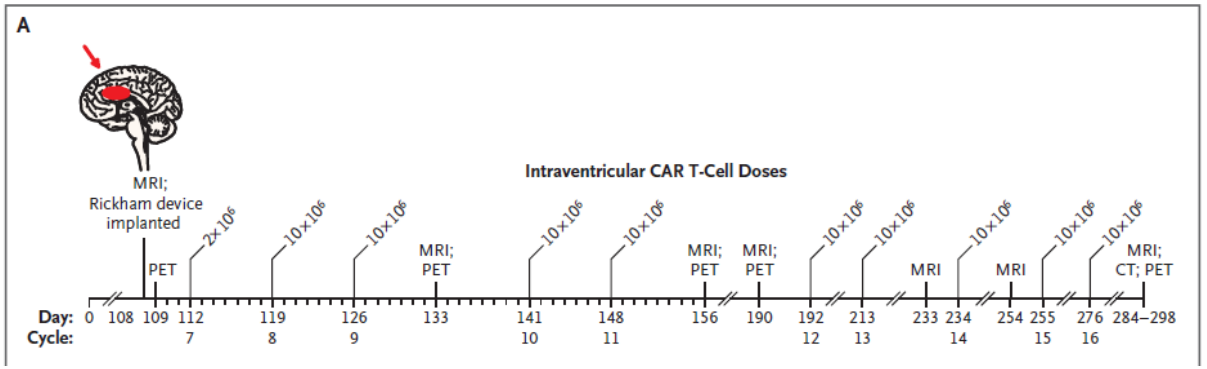
Regression of Glioblastoma after Chimeric Antigen Receptor T-Cell Therapy

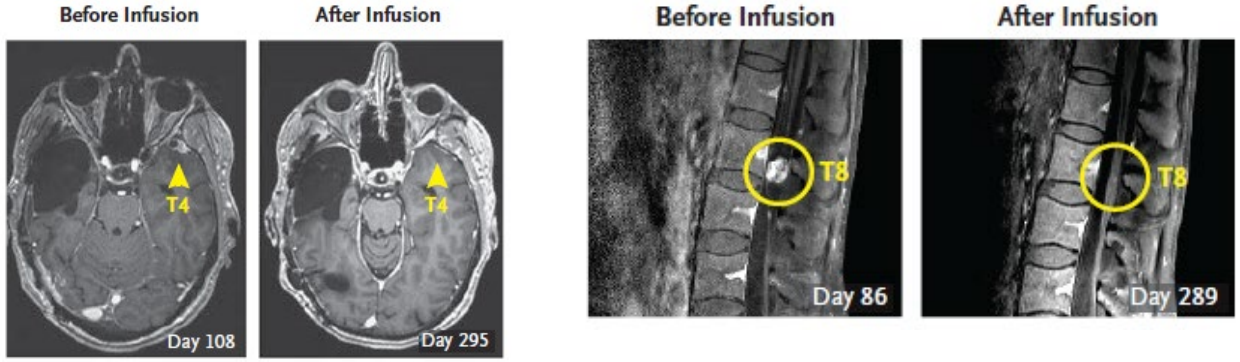
Christine E. Brown, Ph.D., Darya Alizadeh, Ph.D., Renate Starr, M.S., Lihong Weng, M.D., Jamie R. Wagner, B.A., Araceli Naranjo, B.A., Julie R. Ostberg, Ph.D., M. Suzette Blanchard, Ph.D., Julie Kilpatrick, M.S.N., Jennifer Simpson, B.A., Anita Kurien, M.B.S., Saul J. Priceman, Ph.D., Xiuli Wang, M.D., Ph.D., Todd L. Harshbarger, M.D., Massimo D'Apuzzo, M.D., Julie A. Ressler, M.D., Michael C. Jensen, M.D., Michael E. Barish, Ph.D., Mike Chen, M.D., Ph.D., Jana Portnow, M.D., Stephen J. Forman, M.D., and Behnam Badie, M.D.



Intracavitary Delivery of IL13aR2 CAR T Cells

Intraventricular Delivery of IL13aR2 CAR T Cells





Regression of Recurrent Multifocal Glioblastoma, Including Spinal Metastases

EGFR CAR T Cells for GBM: Continued Improvements to Overcome Technical Challenges

IMMUNOTHERAPY

Rational development and characterization of humanized anti–EGFR variant III chimeric antigen receptor T cells for glioblastoma

Laura A. Johnson,[1,2]* John Scholler,[1]* Takayuki Ohkuri,[3] Akemi Kosaka,[3] Prachi R. Patel,[1] Shannon E. McGettigan,[1] Arben K. Nace,[4] Tzvete Dentchev,[4] Pramod Thekkat,[5] Andreas Loew,[5] Alina C. Boesteanu,[1] Alexandria P. Cogdill,[1] Taylor Chen,[1] Joseph A. Fraietta,[1] Christopher C. Kloss,[1] Avery D. Posey Jr.,[1] Boris Engels,[5] Reshma Singh,[5] Tucker Ezell,[5] Neeraja Idamakanti,[5] Melissa H. Ramones,[5] Na Li,[5] Li Zhou,[5] Gabriela Plesa,[1] John T. Seykora,[4] Hideho Okada,[6] Carl H. June,[1,2] Jennifer L. Brogdon,[5] Marcela V. Maus[1,7†]

nature biotechnology

ARTICLES

https://doi.org/10.1038/s41587-019-0192-1

CAR-T cells secreting BiTEs circumvent antigen escape without detectable toxicity

Bryan D. Choi[1,2], Xiaoling Yu[1], Ana P. Castano[1], Amanda A. Bouffard[1], Andrea Schmidts[1], Rebecca C. Larson[1], Stefanie R. Bailey[1], Angela C. Boroughs[1], Matthew J. Frigault[1,3], Mark B. Leick[1], Irene Scarfò[1], Curtis L. Cetrulo[4], Shadmehr Demehri[5], Brian V. Nahed[2], Daniel P. Cahill[2], Hiroaki Wakimoto[2], William T. Curry[2], Bob S. Carter[2] and Marcela V. Maus[1,3*]

CANCER

A single dose of peripherally infused EGFRvIII-directed CAR T cells mediates antigen loss and induces adaptive resistance in patients with recurrent glioblastoma

Donald M. O'Rourke,[1] MacLean P. Nasrallah,[2]* Arati Desai,[3]* Jan J. Melenhorst,[4]* Keith Mansfield,[5]* Jennifer J. D. Morrissette,[6] Maria Martinez-Lage,[2†] Steven Brem,[1] Eileen Maloney,[1] Angela Shen,[7] Randi Isaacs,[5] Suyash Mohan,[8] Gabriela Plesa,[4] Simon F. Lacey,[4] Jean-Marc Navenot,[4] Zhaohui Zheng,[4] Bruce L. Levine,[4] Hideho Okada,[9] Carl H. June,[4] Jennifer L. Brogdon,[5] Marcela V. Maus[10‡]

Choi *et al. Journal for ImmunoTherapy of Cancer* (2019) 7:304
https://doi.org/10.1186/s40425-019-0806-7

Journal for ImmunoTherapy of Cancer

SHORT REPORT Open Access

CRISPR-Cas9 disruption of PD-1 enhances activity of universal EGFRvIII CAR T cells in a preclinical model of human glioblastoma

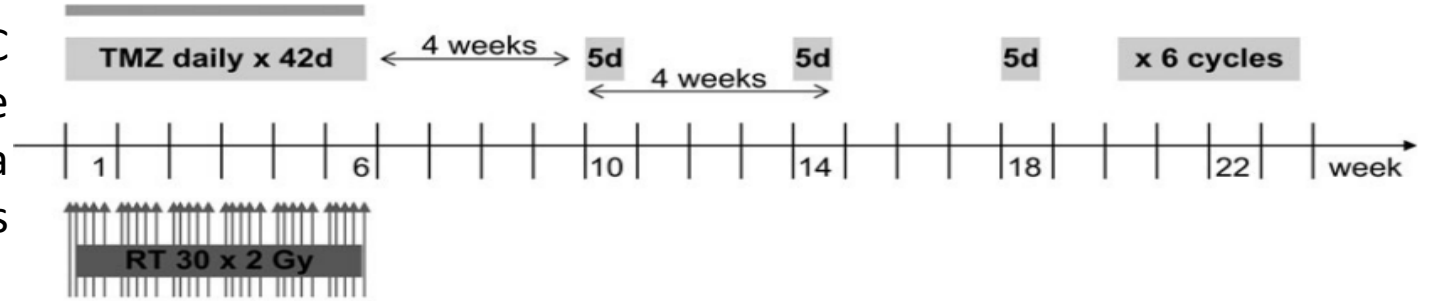
Bryan D. Choi[1,2], Xiaoling Yu[1], Ana P. Castano[1], Henia Darr[3], Daniel B. Henderson[3], Amanda A. Bouffard[1], Rebecca C. Larson[1], Irene Scarfò[1], Stefanie R. Bailey[1], Genevieve M. Gerhard[1], Matthew J. Frigault[1,4], Mark B. Leick[1], Andrea Schmidts[1], Jason G. Sagert[3], William T. Curry[2], Bob S. Carter[2] and Marcela V. Maus[1,4*]

Lessons from GBM Treatment Failures: Challenges to Overcome for New Immunotherapeutic Protocols

- Trusted therapeutic targets expressed in treatment-naïve, primary GBM may be selected against and evolve out of GBM recurrence: new therapeutic targets must be pursued that are relevant to recurrence.
- Monotherapies will not likely succeed in eradicating such a rapidly evolving, highly heterogeneous tumor: rational combinatorial polytherapies should be developed.
- Therapeutics should target not only the GBM cells but also the tumor microenvironment, and to overcome the immunosuppressive niche, the tumour immune microenvironment (TIME)
- Locoregional delivery of immunotherapies (especially into CSF spaces) has been well tolerated and may promote better trafficking, durability and persistence of cell therapies

Mimicking GBM recurrence: Designing mouse-adapted *in vivo* tumor treatment protocol

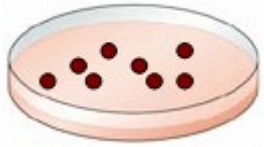
EORTC/NCIC treatment scheme for glioblastoma patients



RT; focal radiotherapy, 60 Gy in 6 weeks to tumor volume + 2-3 cm margin

TMZ; Temozolomide (Temodal®, Temodar®),
During RT: 75 mg/m^2 daily (including weekends) for up to 49 days.
Administration 1-2 hours before RT or in a.m. on days without RT.
Antiemetics: metoclopramide, usually needed only before initial doses.
Maintenance: 150-200 mg/m^2 daily x 5, for up to 6 cycles
Antiemetic prophylaxis with 5HT3 antagonist or metoclopramide

Immunodeficient mouse



Patient-derived primary GBMs

Cranial Radiation
TMZ (single dose) as sensitizer for radiation
1 hour pre-radiation

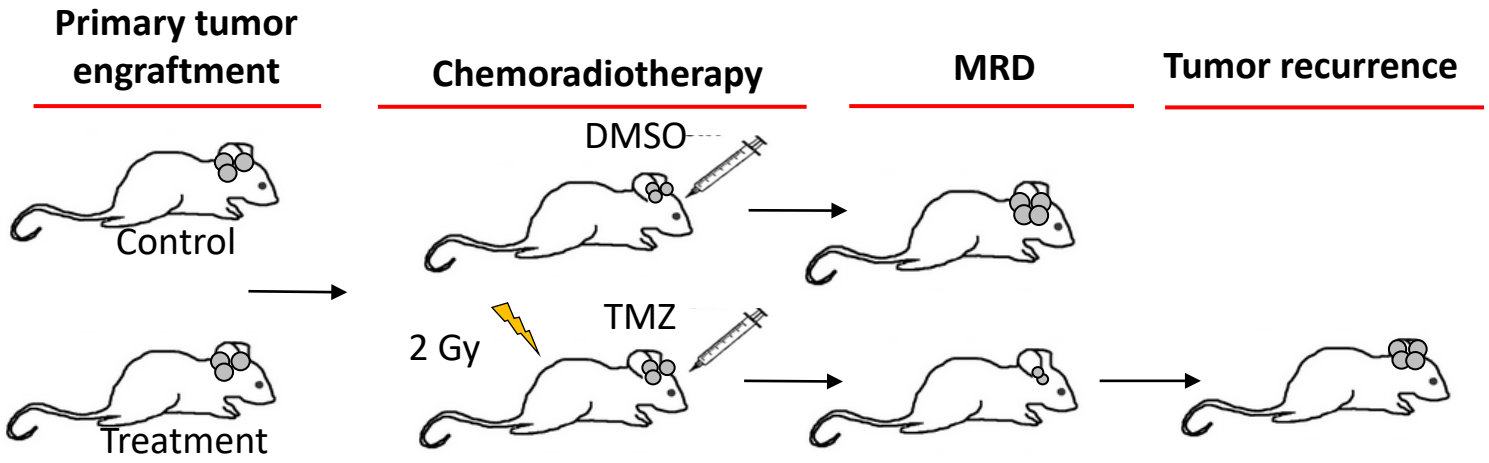
TMZ (single dose)

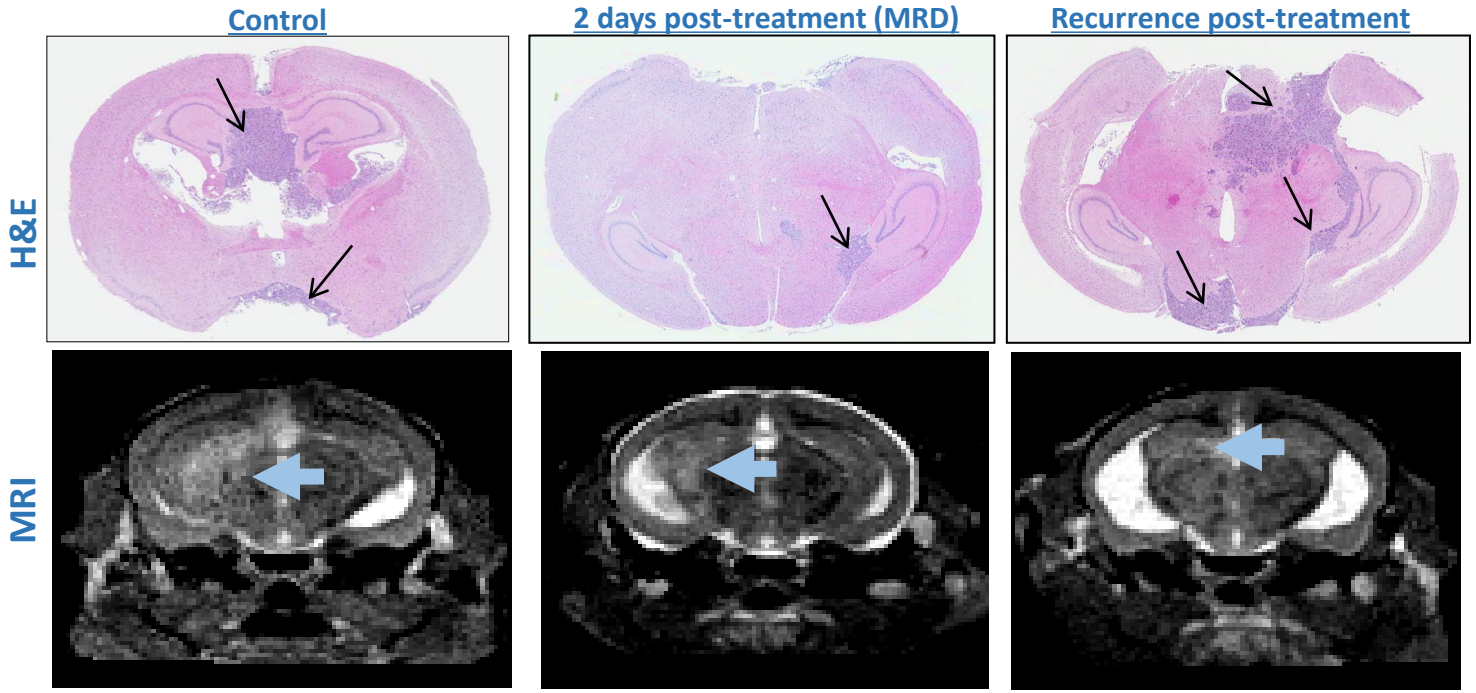
TMZ (single dose)

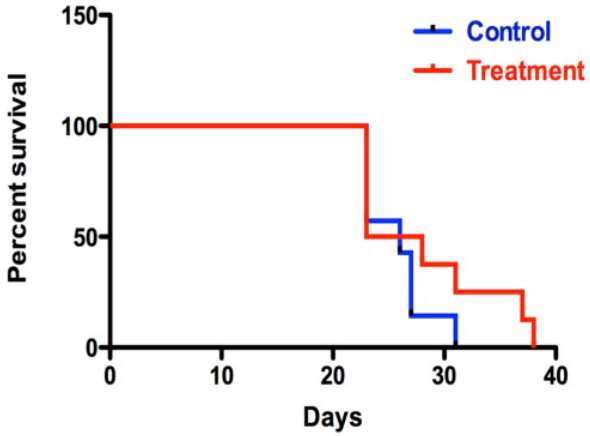
Sacrifice Day (MRD)

Sacrifice Day

Preclinical model of recurrent GBM







GBM program: A Translational Pipeline

Targeting clonal heterogeneity in treatment-refractory GBM with novel and empiric immunotherapies

PROJECT 1: Clonal dynamics and tracking
Dr. Jason Moffat

Discover and validate novel cell surface markers of recurrent GBM

CORE 3: Platform for Advanced Cell Engineering

PROJECT 2: Engineering biologics
Drs. Henry/Sidhu

Build and validate immunotherapeutic modalities targeting surface markers of recurrent GBM

CORE 2: Antibody Engineering Facility

PROJECT 3: Targeting heterogeneity in GBM
Dr. Sheila Singh

Early development/validation of immuno-therapeutic modalities targeting recurrent GBM in patient-derived models

CORE 1: Preclinical/Animal Facility

EMPIRICA Therapeutics

CENTURY THERAPEUTICS

- Late preclinical development
- Method development & validation
- Clinical Product development (large-scale, non-GMP manufacturing)

CD133, a marker of tumor initiating cells


Sheila Singh


Jason Moffat

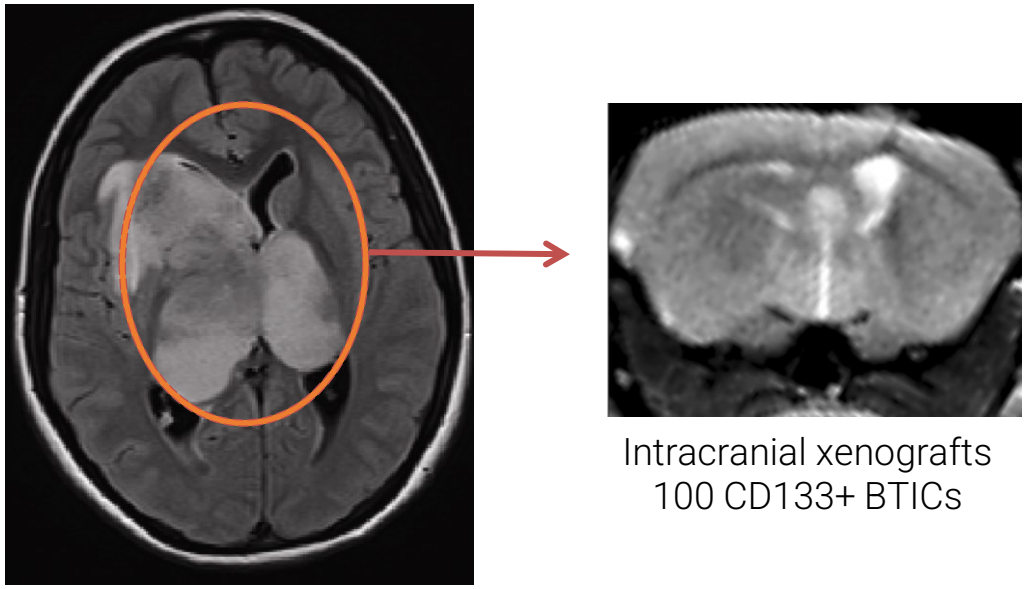

Parvez Vora


Chitra Venugopal

Nature **432**, 396-401 (18 November 2004) | doi:10.1038/nature03128; Received 7 September 2004; Accepted 22 October 2004

Identification of human brain tumour initiating cells

Sheila K. Singh[1,2,3], Cynthia Hawkins[1,4], Ian D. Clarke[1,2], Jeremy A. Squire[6], Jane Bayani[6], Takuichiro Hide[1,2], R. Mark Henkelman[5], Michael D. Cusimano[3,7] & Peter B. Dirks[1,2,3]



Intracranial xenografts
100 CD133+ BTICs

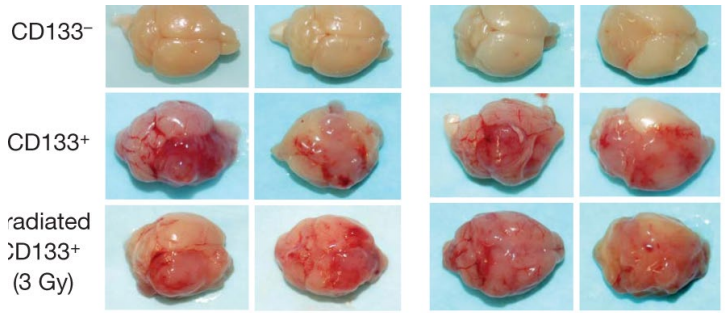
Brain Tumor Initiating Cell (BTIC) model

Tumor Type	Marker(s) Used to Enrich for CSCs
Acute myeloid leukemia	$CD34^+CD38^-$
Breast	$CD44^+$ $CD24^-$
Breast	$ALDH1^+$
Brain	$CD133^+$
Prostate	$CD44^+$ $\alpha_2\beta_1^{high}$ $CD133^+$
Head and neck	$CD44^+$
Colon	$CD133^+$
Colon	$EpCAM^{high}$ $CD44^+$
Colon	$ALDH1^+$
Pancreas	ESA^+CD44^+ $CD24^+$
Pancreas	$CD133^+$
Mesenchymal	Side population
Lung	$CD133^+$
Liver	$CD90^+$
Melanoma	$ABCB5^+$
Ovarian	$CD133^+$

CD133, a marker of treatment-resistance in several human malignancies

O'Brien et al 2010, Clin. Can. Res.

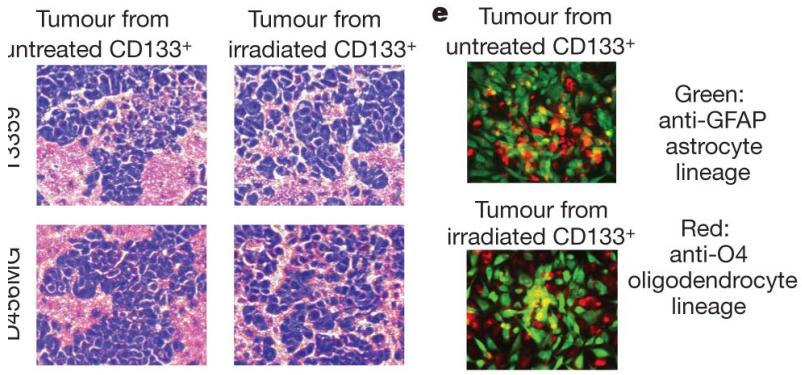
CD133, a marker of treatment-resistant GBM



Nature **444**, 756-760 (7 December 2006) | doi:10.1038/nature05236; Received 1 June 2006; Accepted 7 September 2006; Published online 18 October 2006

Glioma stem cells promote radioresistance by preferential activation of the DNA damage response

Shideng Bao[1,2], Qiulian Wu[1,2], Roger E. McLendon[2,3], Yueling Hao[1,2], Qing Shi[1,2], Anita B. Hjelmeland[1,2], Mark W. Dewhirst[4], Darell D. Bigner[2,3] & Jeremy N. Rich[1,2,5,6]



Molecular Cancer

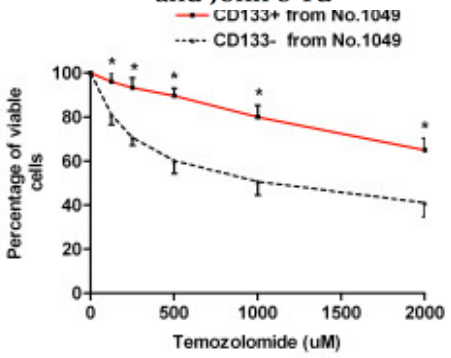
BioMed Central

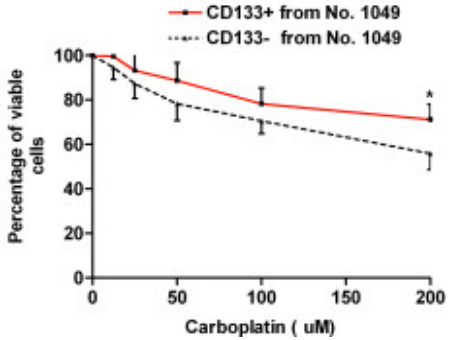
Research

Open Access

Analysis of gene expression and chemoresistance of CD133⁺ cancer stem cells in glioblastoma

Gentao Liu[1,2], Xiangpeng Yuan[1], Zhaohui Zeng[1], Patrizia Tunici[1], Hiushan Ng[1], Iman R Abdulkadir[1], Lizhi Lu[1,3], Dwain Irvin[1], Keith L Black[1] and John S Yu*[1,4]





CD133 expression correlates with disease progression, metastasis, recurrence, and poor overall survival in several human malignancies

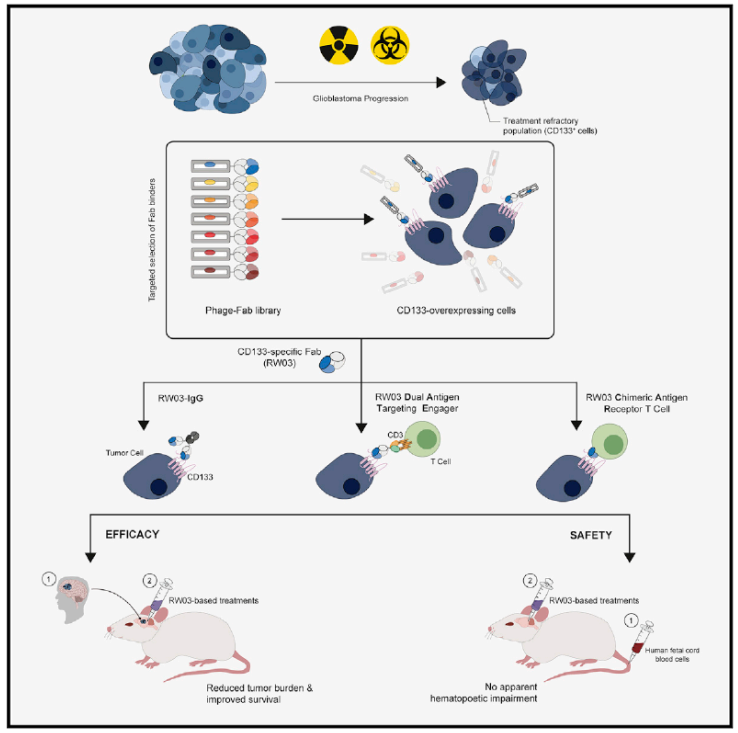
Engineering CD133-targeting immunotherapies

Cell Stem Cell

Clinical and Translational Report

The Rational Development of CD133-Targeting Immunotherapies for Glioblastoma

Graphical Abstract



Authors

Parvez Vora, Chitra Venugopal, Sabra Khalid Salim, ..., Kristin Hope, Jason Moffat, Sheila Singh

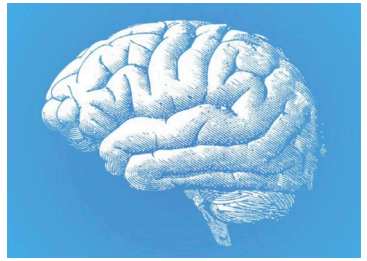
Correspondence

ssingh@mcmaster.ca (S.S.), j.moffat@utoronto.ca (J.M.)

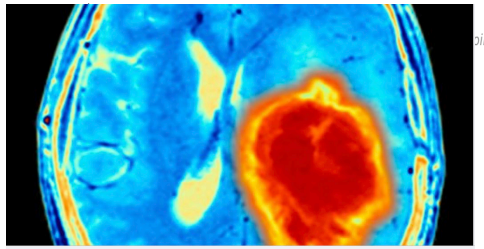
In Brief

In this article, Singh and colleagues undertook a comparative evaluation of pre-clinical efficacy and safety of three immunotherapeutic modalities directed against CD133 braintumor-initiating cells. While all three modalities were efficacious in orthotopic GBM xenografts, CD133-specific CAR-T cells represented the most therapeutically tractable strategy against functionally important CD133+ GBM cells.

FIERCE Biotech



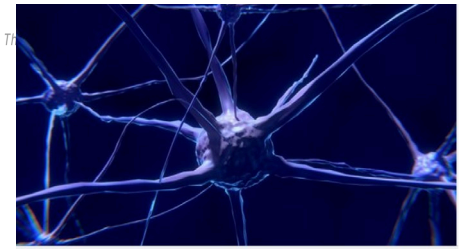
Startup targets glioblastoma tumors with CAR-T therapy



GENENGNEWS.COM

CAR-T Cell Therapy Shows Promise against Glioblastoma in Mice

Study results have led to establishment of brain cancer immunotherapy…



MEDICALXPRESS.COM

Treatment shows promise in treating deadly brain cancer

Researchers of McMaster University and the University of Toronto have…

SCIENMAG.COM

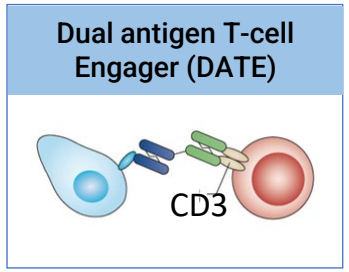
Treatment shows promise in treating deadly brain cancer l Scienmag: Latest Science and Health News

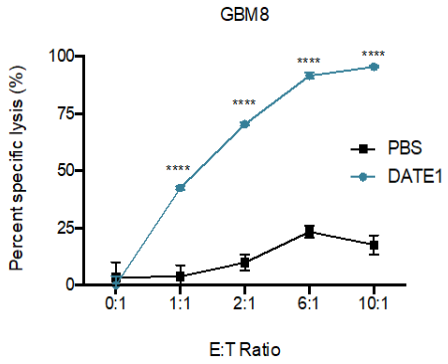
When used in mice with human glioblastoma, CD133-targetting CAR-T therapy was considered a success Hamilton, ON (May 27, 2020) - Researchers of McMaster University and the University of Toronto have developed a promising…

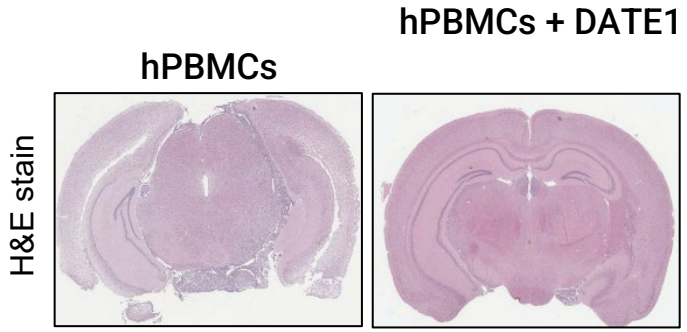
CENTURY THERAPEUTICS

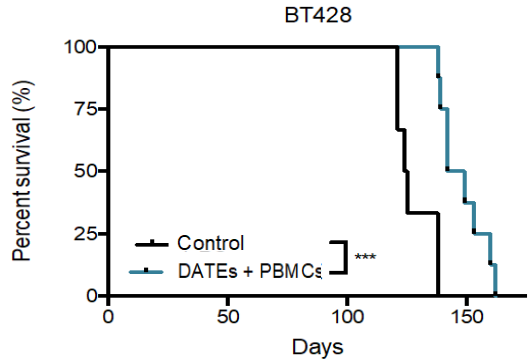
EMPIRICA Therapeutics 25

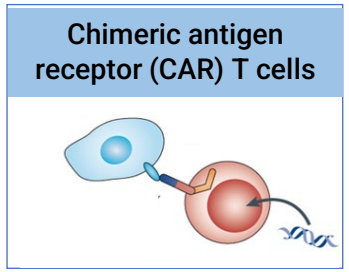
CD133-directed treatment significantly eliminates GBM tumor burden

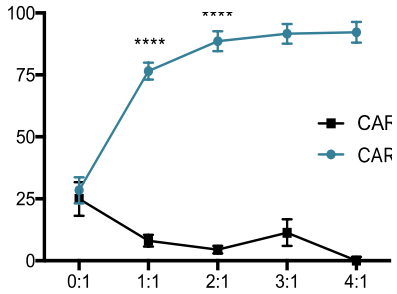


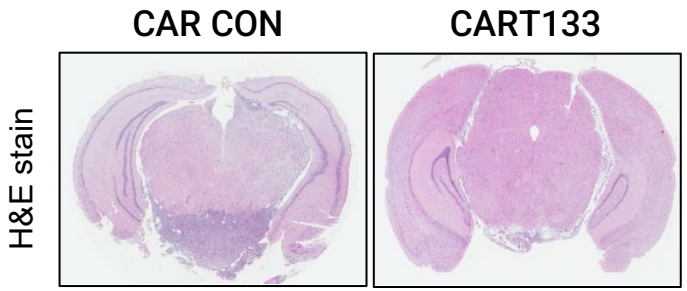


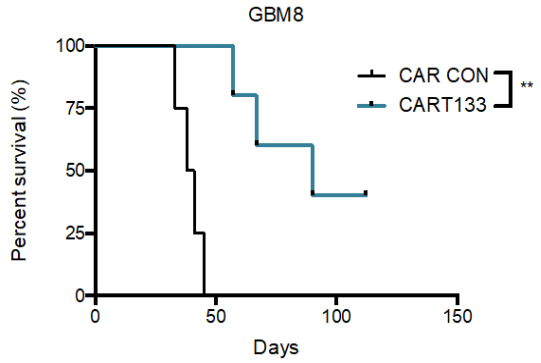








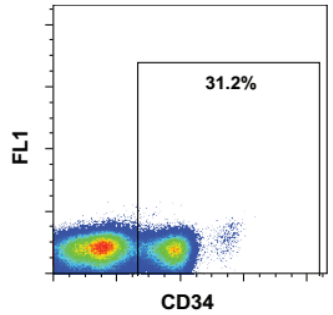




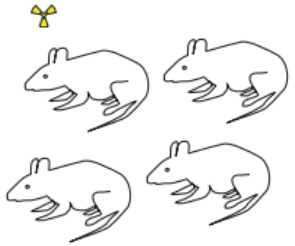
Vora *et al.,* 2020 Cell Stem Cell

Measuring the ‘ON target OFF tumor’ effect in humanized NSG mice

Hematopoietic stem cell enrichment from Lin-cord blood



Transplant 15,000 CD34+ cells/mouse



NSG

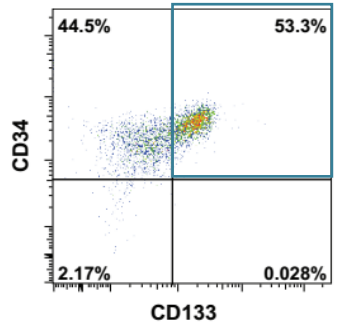
12wk

Long-term human stem cell repopulation

2wk

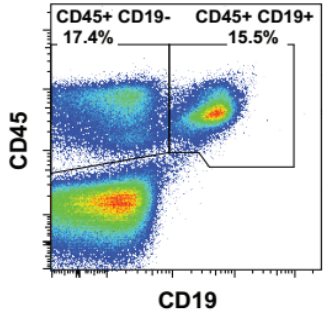
CD133 DATEs CART133 cell treatment Intracranial or IV Delivery

Assess bone marrow for changes in CD133+ hematopoietic stem and progenitor cell levels

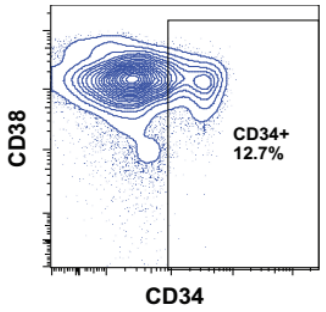


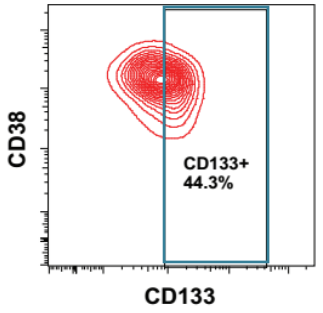
Validate CD133 expression in cord blood HSPCs pre-transplant

Bone marrow aspiration



Bone marrow engraftment

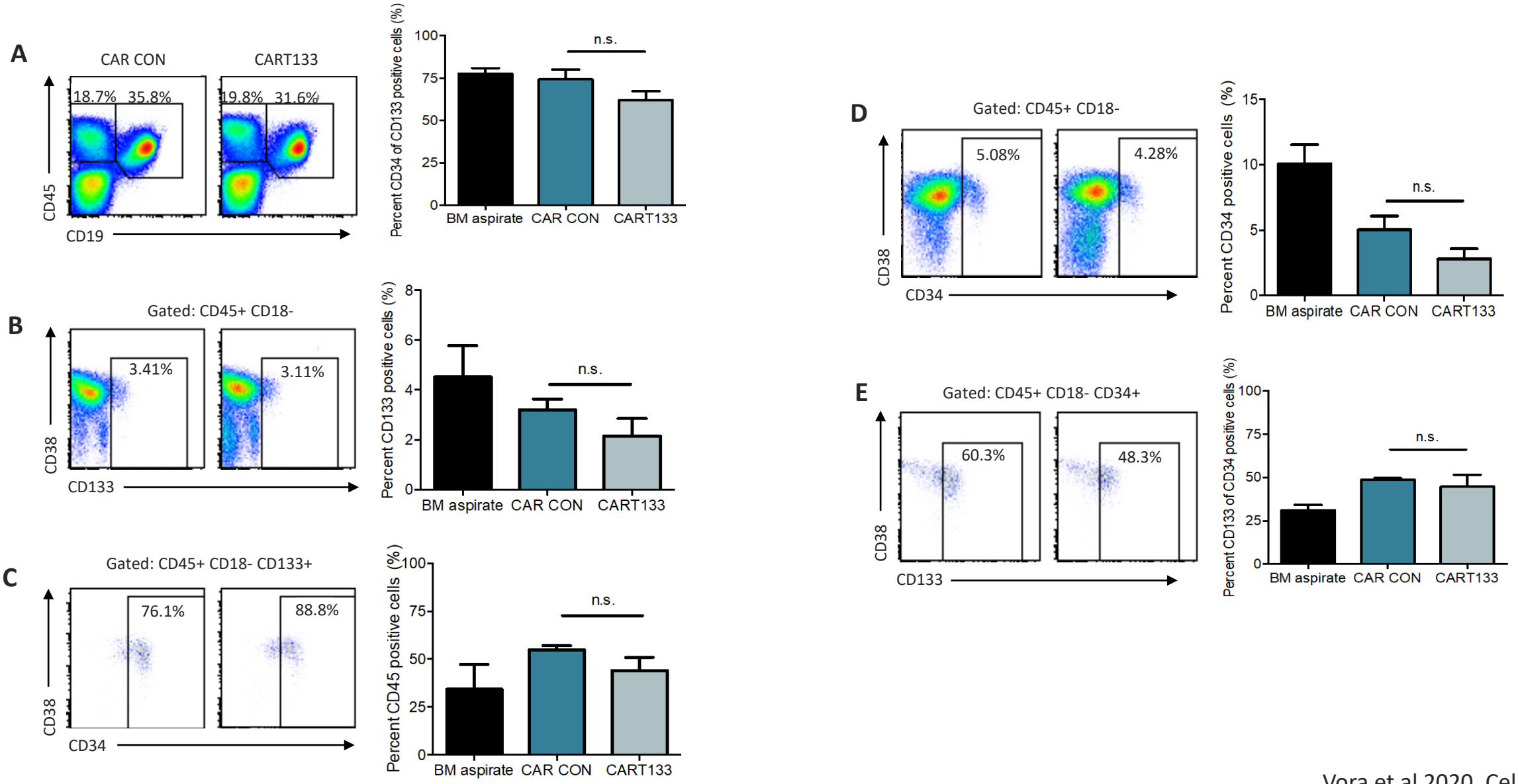




CD133 expression in bone marrow pre-treatment

Vora et al 2020 Cell Stem Cell

ET001 treatment does not significantly reduce numbers of human HSPCs or impair haematopoiesis



Vora et al 2020, Cell Stem Cell

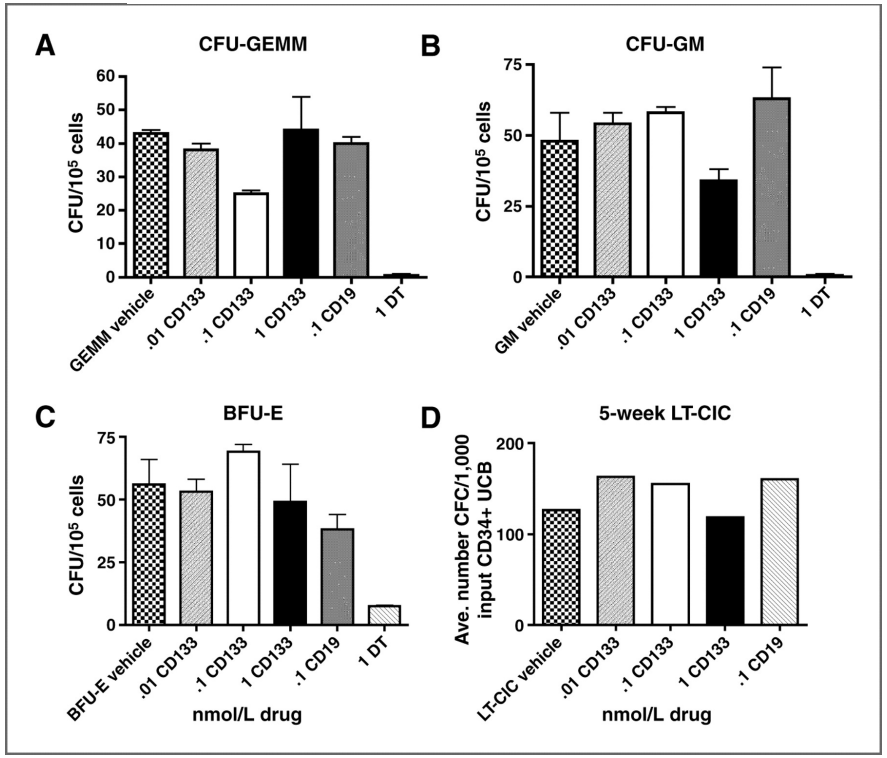
CD133 plays a redundant role in haematopoiesis?

Therapeutic Discovery

Molecular Cancer Therapeutics

Targeting Tumor-Initiating Cancer Cells with dCD133KDEL Shows Impressive Tumor Reductions in a Xenotransplant Model of Human Head and Neck Cancer

Nate N. Waldron[1], Dan S. Kaufman[2], Seunguk Oh[3], Zintis Inde[3], Melinda K. Hexum[2], John R. Ohlfest[4], and Daniel A. Vallera[3]



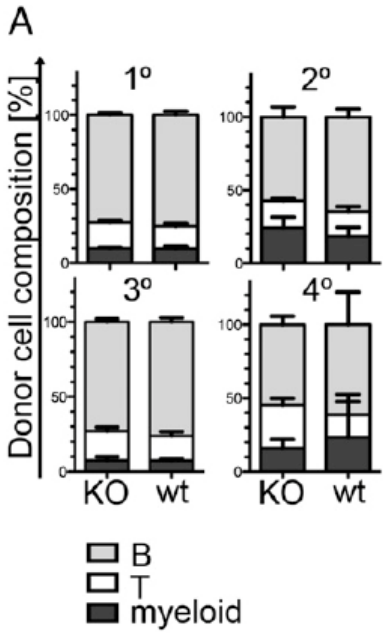
"CD133+ cell targeting using dCD133KDEL does not inhibit hematopoietic colony development as assessed by short-term (2-weeks) and long-term (5-weeks) culture and colony-forming assays"

PNAS

CD133 is a modifier of hematopoietic progenitor frequencies but is dispensable for the maintenance of mouse hematopoietic stem cells

Kathrin Arndt[a], Tatyana Grinenko[a], Nicole Mende[a], Doreen Reichert[b], Melanie Portz[a], Tatsiana Ripich[a,1], Peter Carmeliet[c,d], Denis Corbeil[b], and Claudia Waskow[a,2]

[a]Regeneration in Hematopoiesis, Center for Regenerative Therapies Dresden (CRTD), Technische Universität Dresden, 01307 Dresden, Germany; [b]Tissue Engineering Laboratories, Biotec, and CRTD, Technische Universität Dresden, 01307 Dresden, Germany; [c]Laboratory of Angiogenesis and Neurovascular Link, Vesalius Research Center, VIB, 3000 Leuven, Belgium; and [d]Laboratory of Angiogenesis and Neurovascular Link, Department of Oncology, Katholieke Universiteit Leuven, 3000 Leuven, Belgium



"CD133-deficient HSCs (KO) can competitively and serially reconstitute immune cells and the HSC compartment of irradiated recipient mice"

"Animals were viable and fertile but are affected with a retinal degeneration leading to blindness. No obvious hematopoietic defects were reported in CD133 KO mice"

NCT02541370: a phase I clinical trial of CD133-specific CAR-T for treatment of relapsed and/or chemotherapy refractory advanced malignancies

Participant Overview [n=23]

- 7 with pancreatic carcinomas
- 2 with colorectal carcinomas
- 14 with hepatocellular carcinoma (HCC)

Dose escalation study results:

- Dose 1: Primary dose (0.05-0.15 x 10^6 cells/kg) was not sufficient in creating an obvious decrease in CD133 cells and an increase in CAR-gene copy
- Dose 2: Four patients moved onto dose 2(0.05-1.0 x 10^6 cells/kg) in cohort 2.These patients experienced mild (≤ Grade 2) hematologic toxicities but **self-recovered within 1 week.** CD133+ decreased and CAR-gene copy number increased
- Dose 3: The CART-133 cell dose was increased to 1.0-2.0 × 10^6/kg for patients 5 to 8 in cohort 3. Similar toxicities and effective activity were all observed in cohort 3

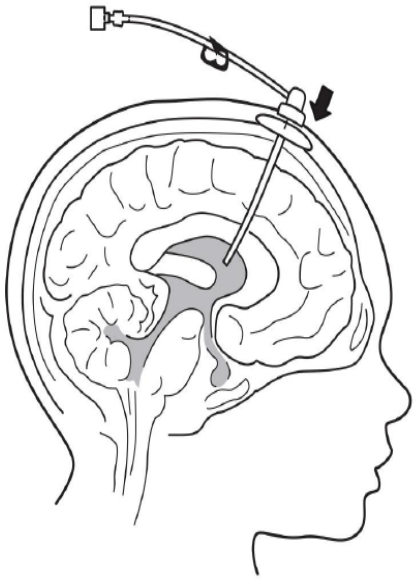
Table 2. Patients' response and toxicity.

			Outcome		Grade ≥ 2 toxicities			
Patient No.	Disease status at study entry	No. of CAR positive T cells infused (10^6/kg) at each treatment cycle	Response (month)	New metastatic lesions during treatment	Adverse events	Grade	Time of occurrence after cell infusion	Duration
1	PD	1 st: 0.78	SD (4.25)	None	None			
2	PD	1 st: 0.51	PD	Spleen	Nausea Constipation	II II	2 weeks 2 weeks	2 weeks 2 weeks
3	PD	1 st: 0.8	SD (3.5)	None	None			
4	PD	1 st:0.67	SD (3)	None	Anemia	II	3 days	1 week
					Thrombocytopenia	II	3 days	1 week
					Hyperbilirubinemia	III	5 days	3 weeks
5	PD	1 st: 1.01; 2 nd: 0.6	SD (4.5)	None	None			
6	PD	1 st: 1.0; 2 nd: 0.5 3rd:1.4; 4th:1.6	SD (15.25)	None	None			
7	PD	1 st: 1.8; 2 nd: 0.83 3rd:1.5	SD (4)	None	Hypotesion	II	2 days	2-3days
8	PD	1 st: 1.98; 2 nd: 0.52; 3rd: 1.34	PR (3) SD(1.7)	Abdominal wall	None			
9	PD	1 st: 1.32	PD	None	Hyperbilirubinemia	III	3 weeks	3 weeks
10	PD	1 st: 0.67; 2 nd: 1.43; 3rd: 1.08	PD	None	None			
11	PD	1 st: 1.05	SD (2)	None	None			
12	PD	1 st: 2.0; 2 nd:2.0 3rd: 1.5	SD (13.7+)	None	None			
13	PD	1 st: 0.85	PD	None	None			
14	PD	1 st: 1.8; 2 nd: 1.0 3rd: 0.8	SD (6)	None	None			
15	PD	1 st: 1.48; 2 nd:1.67 3rd: 2.0	PR (4)	None	Leukopenia	IV	2 days	2 weeks
16	PD	1 st:1.88; 2 nd:1.67 3rd: 1.92	PR (2)	None	Leukopenia Thrombocytopenia	III II	2 days 2 days	2-3 days 2–3 days
17	PD	1 st: 2.0	SD (3)	None	Thrombocytopenia	II	2-5days	3 weeks
18	PD	1 st: 1.8	SD (3)	None	Leukopenia	II	2 days	2-5 days
19	PD	1 st: 1.38	PD	None	Leukopenia	II	2-5days	1 week
		2 nd:1.67			Anemia	II	2–5days	2 weeks
					Nausea	III	2 weeks	4 weeks
					Anorexia	II	2 weeks	4 weeks
					Mucosa hyperemia	II	4 weeks	2 weeks
20	PD	1 st: 1.72	PD	None	Leukopenia	II	2-5days	1 week
					Anemia	III	2–5 days	2 weeks
					Nausea	II	2 weeks	4 weeks
					Anorexia	II	2 weeks	4 weeks
					Mucosa hyperemia	II	4 weeks	2 weeks
21	PD	1 st:1.43; 2 nd: 1.78 3rd:1.52	SD (10.25+)	None	Leukopenia	II	2-5days	2-5 days
22	PD	1 st:1.87	SD (2.2)	None	Leukopenia	II	2-5days	2 weeks
					Hyperbilirubinemia (Direct bilirubin)	III	1 week	3 weeks
23	PD	1 st:1.43; 2 nd:1.79	SD (15.7+)	None	Leukopenia	III	2-5days	1 week

Abbreviations: PR, regression of measurable disease (≥30% decrease) and no new sites; SD, stable disease; PD, progressive disease.

Wang et al 2018, Oncoimmunology

Locoregional delivery can address CAR-T trafficking challenges



Holter™ Rickham Catheter device for infusion of CAR-T cells

Ongoing Phase 1 CAR-T clinical trials utilizing intracranial route of administration

Identifier	Indication	Therapy	Sponsor
NCT02208362	Relapsed GBM	Anti-IL13Ra2 CAR-T	City of Hope Medical Center
NCT03283631	Relapsed GBM	Anti-EGFRvIII CAR-T	Duke University Medical Center
NCT02442297	Relapsed GBM	Anti-HER2 CAR-T	Baylor College of Medicine
NCT03696030	Recurrent Brain or leptomeningeal Metastases	Anti-HER2 CAR-T	Baylor College of Medicine
NCT03500991	Recurrent/refractory pediatric CNS Tumors	Anti-HER2 CAR-T	Seattle Children's Hospital
NCT03638167	Recurrent/refractory pediatric CNS Tumors	Anti-EGFR806 CAR-T	Seattle Children's Hospital
NCT04003649	Recurrent/refractory GBM	Anti-IL13Ra2 CAR-T + nivolumab (IV)	City of Hope Medical Center
NCT03389230	Recurrent/refractory high-grade Glioma	Anti-HER2 memory-enriched T cells	City of Hope Medical Center

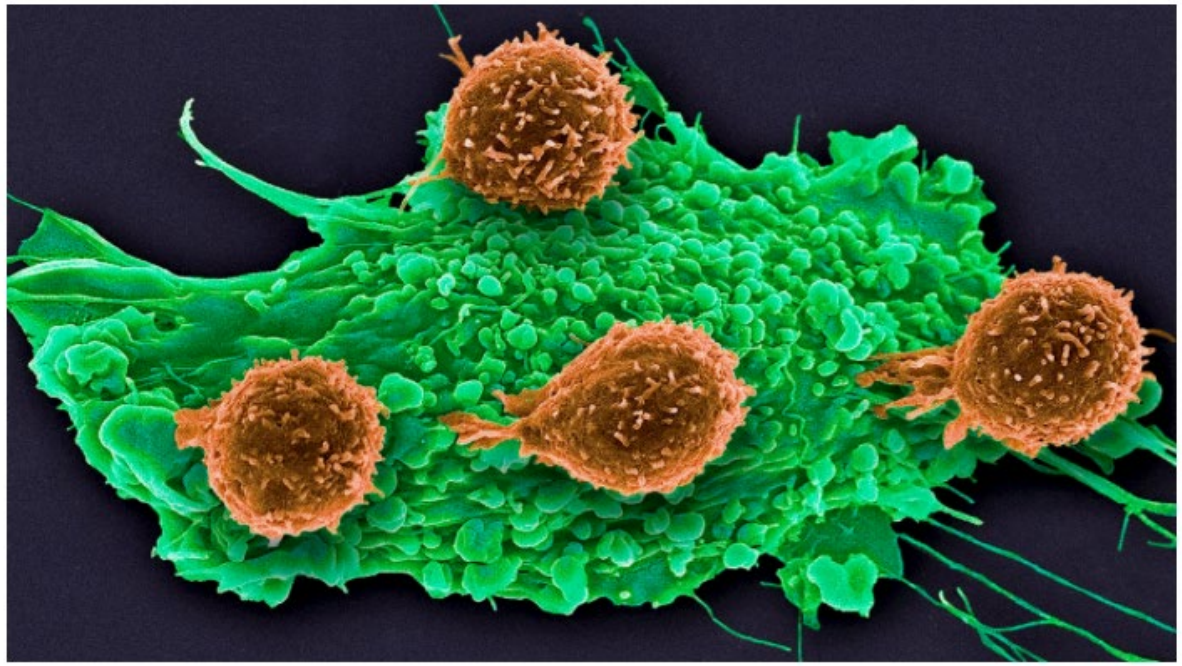
Engineering new allogeneic CAR T therapies for cancer patients

RESEARCH ARTICLE SUMMARY

CLINICAL TRIALS

CRISPR-engineered T cells in patients with refractory cancer

Edward A. Stadtmauer*†, Joseph A. Fraietta*, Megan M. Davis, Adam D. Cohen, Kristy L. Weber, Eric Lancaster, Patricia A. Mangan, Irina Kulikovskaya, Minnal Gupta, Fang Chen, Lifeng Tian, Vanessa E. Gonzalez, Jun Xu, In-young Jung, J. Joseph Melenhorst, Gabriela Plesa, Joanne Shea, Tina Matlawski, Amanda Cervini, Avery L. Gaymon, Stephanie Desjardins, Anne Lamontagne, January Salas-Mckee, Andrew Fesnak, Donald L. Siegel, Bruce L. Levine, Julie K. Jadlowsky, Regina M. Young, Anne Chew, Wei-Ting Hwang, Elizabeth O. Hexner, Beatriz M. Carreno, Christopher L. Nobles, Frederic D. Bushman, Kevin R. Parker, Yanyan Qi, Ansuman T. Satpathy, Howard Y. Chang, Yangbing Zhao, Simon F. Lacey*, Carl H. June*†



Immune cells (brown) attack a cancer cell. Using CRISPR could make the immune cells more potent. STEVE GSCHMEISSNER/SCIENCE SOURCE

Cutting-edge CRISPR gene editing appears safe in three cancer patients

By Jennifer Couzin-Frankel | Feb. 6, 2020 , 2:00 PM

CENTURY THERAPEUTICS

Enhanced Control of iNK Cells in the Treatment of GBM

Hy Levitsky, MD I President, R&D

Major Challenges in Cell Therapy for GBM

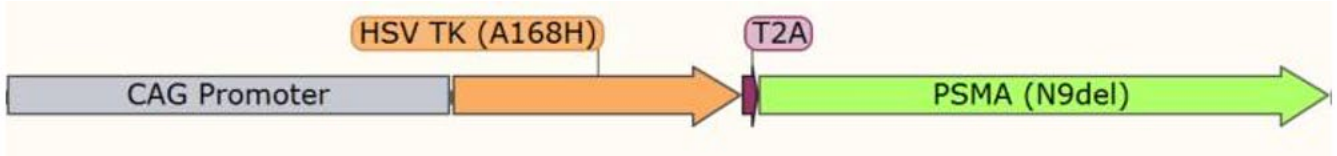
- Clonal evolution of cancer cells driving antigen heterogeneity
- The most abundant target antigens are also expressed at some level on normal tissues
- The CNS is highly sensitive to features associated with immune effector function (e.g., cytokines, rapid cell expansion, altered vascular permeability)
- Difficulty assessing PK and biodistribution of effector cells in the brain complicates dose and schedule optimization
- Suppressive features of the tumor microenvironment must be addressed in product and clinical trial design

The ability to address many of these challenges requires a level of *<u>therapeutic control</u>* that has not been a feature of current generation cell therapies

Century's iNK platform-
Engineered to provide control to overcome these challenges

- NK cells significantly less proliferative than T cells, reducing the risk of toxicities associated with rapid and extensive lymphocyte expansion in the brain
- iNK clones selected for maximal serial killing capacity, achieving tumor eradication with less cell expansion vs CAR-T
- Direct activation of iNK cells via NKG2D recognition of GBM "stress ligands" MIC-A, MIC-B, ULBP
- Antigen heterogeneity addressed with multi-plex targeting via "bridge molecules" (monoclonal antibodies engaging CD16 and custom binders engaging Universal CAR)
  - **Finite half-life of protein bridge molecules provide control over the extent of iNK cell activation against targets**
- HSV-tk enables rapid termination of toxicities unresponsive to SOC
- PET reporter genes designed to enable serial non-invasive assessment of PK and biodistribution to guide dose and schedule during clinical development (and potentially in clinical practice)

HSVtk-2A-PSMA Cassette



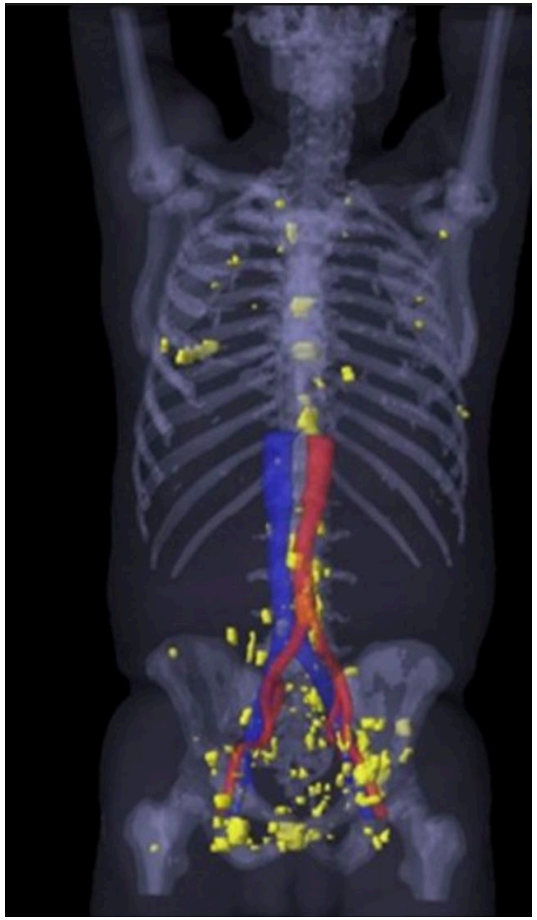
- Single molecular construct enables co-expression and selection for intracellular HSV-tk, and surface membrane expressed PSMA

- HSV-tk encodes an intracellular enzyme that converts ganciclovir (GCV) into GCV-triphosphate that inhibits DNA-polymerase, leading to cell death (“Safety Switch”)
  - Used successfully in the clinic to abort T cell mediated toxicity (GVHD) associated with allogeneic donor lymphocyte infusions[1,2]

- PSMA imaging with clinically approved PET probes is widely used to detect and quantify prostate cancer micro-metastases
  - Preclinical studies of PSMA as a *PET reporter gene* in CAR-T demonstrate sensitive and quantitative detection of CAR-T in sites of accumulation (“total body PK”)

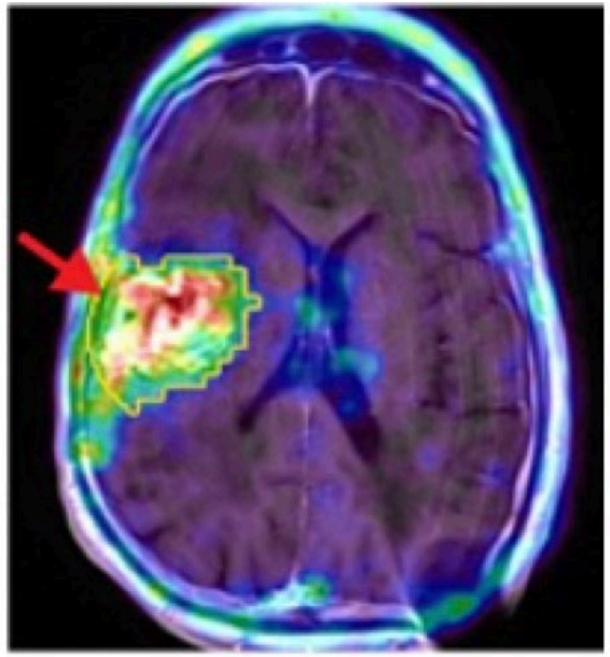
1) Bonini et al., SCIENCE VOL. 276/p1719-24 13 JUNE 1997 and 2) Greco et al., Frontiers in Pharmacology **1** May2015|Volume 6|Article 95

PET Imaging for Quantitative Assessment of Cell Trafficking, Abundance, and Persistence



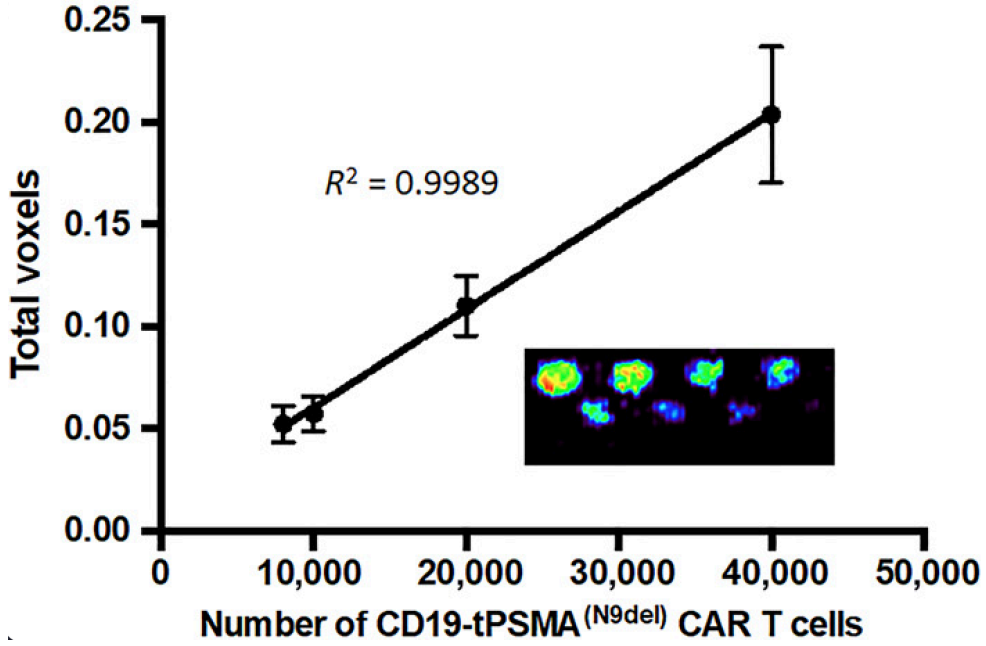
PSMA PET Imaging of Prostate Cancer

OncologyLive, Vol. 21/No. 6, Volume 21, March 13, 2020



HSV-tk PET Imaging of CAR-T in GBM

SCIENCE TRANSLATIONAL MEDICINE
18 Jan 2017 Vol 9,Issue 373



Correlation between PET signal strength and CAR-T accumulation in mouse model

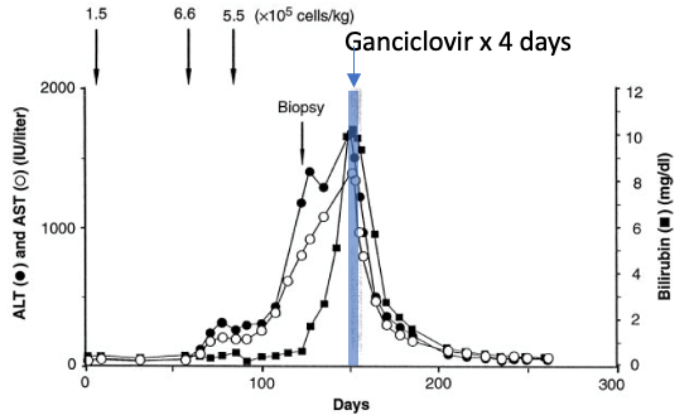
SCIENCE ADVANCES 3 Jul 2019 Vol 5,Issue 7

Safety Switch

- Ability to rapidly eliminate the product upon encountering severe toxicities improves safety profile, broadens eligible patient populations, and partially de-risks pursuing novel targets that may have narrow therapeutic windows
- Transgenic HSV-tk expression has been successfully used in the clinic to abrogate severe T cell mediated toxicities within hours of ganciclovir administration
- Recently, CAR-T associated ICANS and CRS has been successfully abrogated within hours of triggering an alternate safety switch platform (iCas9 + rimiducid)

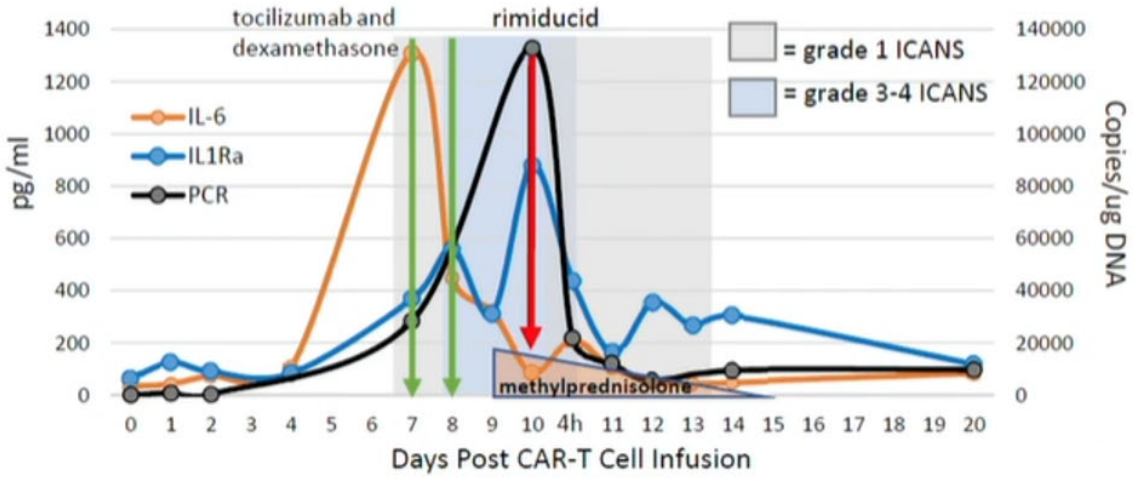
HSV-TK Gene Transfer into Donor Lymphocytes for Control of Allogeneic Graft-Versus-Leukemia

Chiara Bonini, Giuliana Ferrari, Simona Verzeletti, Paolo Servida, Elisabetta Zappone, Luciano Ruggieri, Maurilio Ponzoni, Silvano Rossini, Fulvio Mavilio, Catia Traversari, Claudio Bordignon*



SCIENCE • VOL. 276 • 13 JUNE 1997 • www.sciencemag.org

Safety Switch Activation Rapidly Controls Severe CAR-T Associated ICANS



G. Dotti et al., ASGCT presentation May 2022

Enhanced Control of iNK Cells To Address GBM

- Therapeutic control achieved through engineered product attributes enables the pursuit of the most challenging oncology settings, including GBM

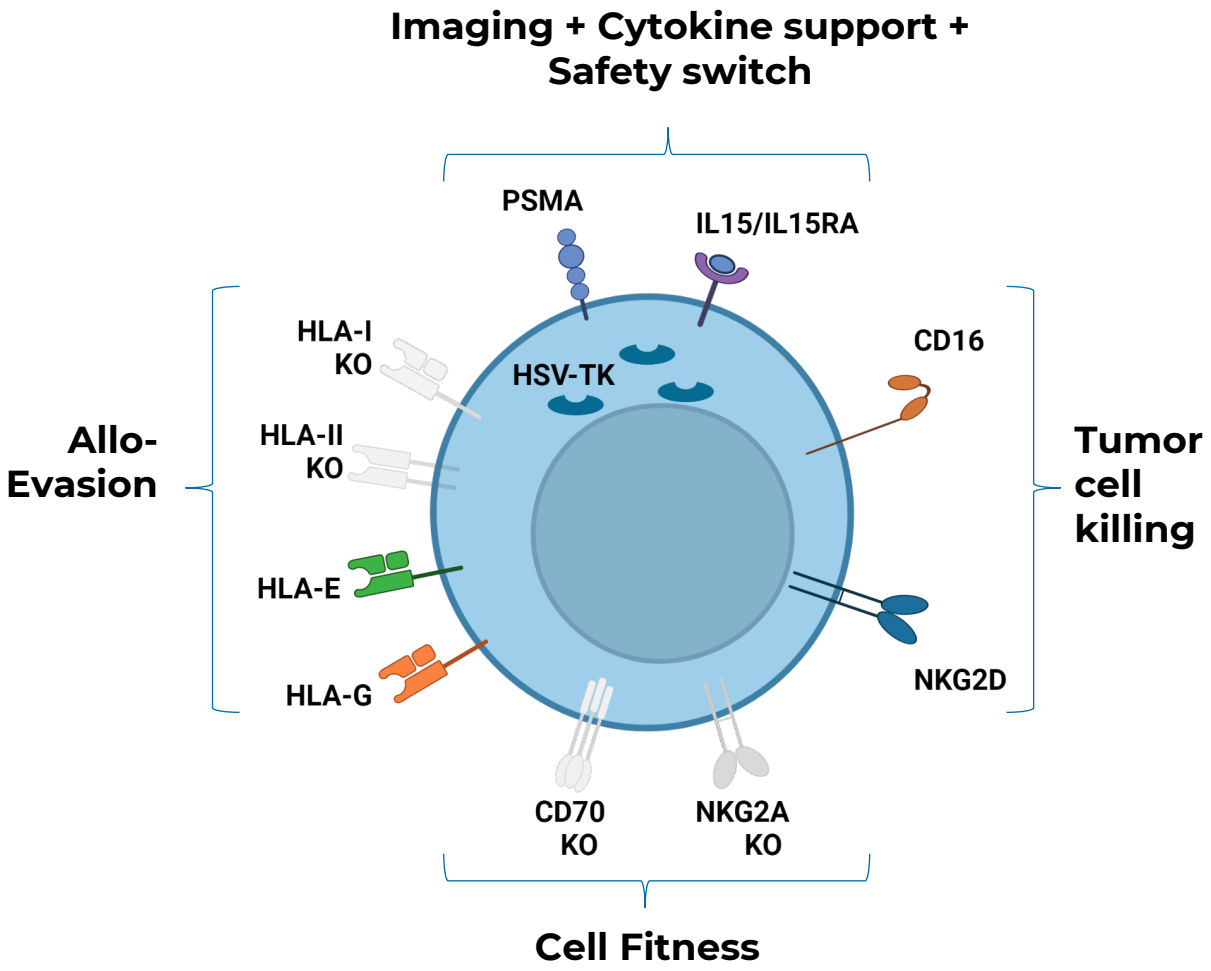
- These attributes include:
  - Selection of cell type (iNK) and clones with limited replicative capacity
  - Tumor targeting via co-administered bridge molecules with finite half-lives
  - Precise assessment of cell expansion, biodistribution, and tissue-resident PK to guide dose and schedule determination
  - Safety switch to abrogate toxicities

CENTURY
THERAPEUTICS

Century's iNK 3.0 platform
iNK common progenitor and Next-Gen CNTY-103

Luis Borges, PhD I CSO

iNK 3.0 Common Progenitor
Multiple New Features for Enhanced Functionality



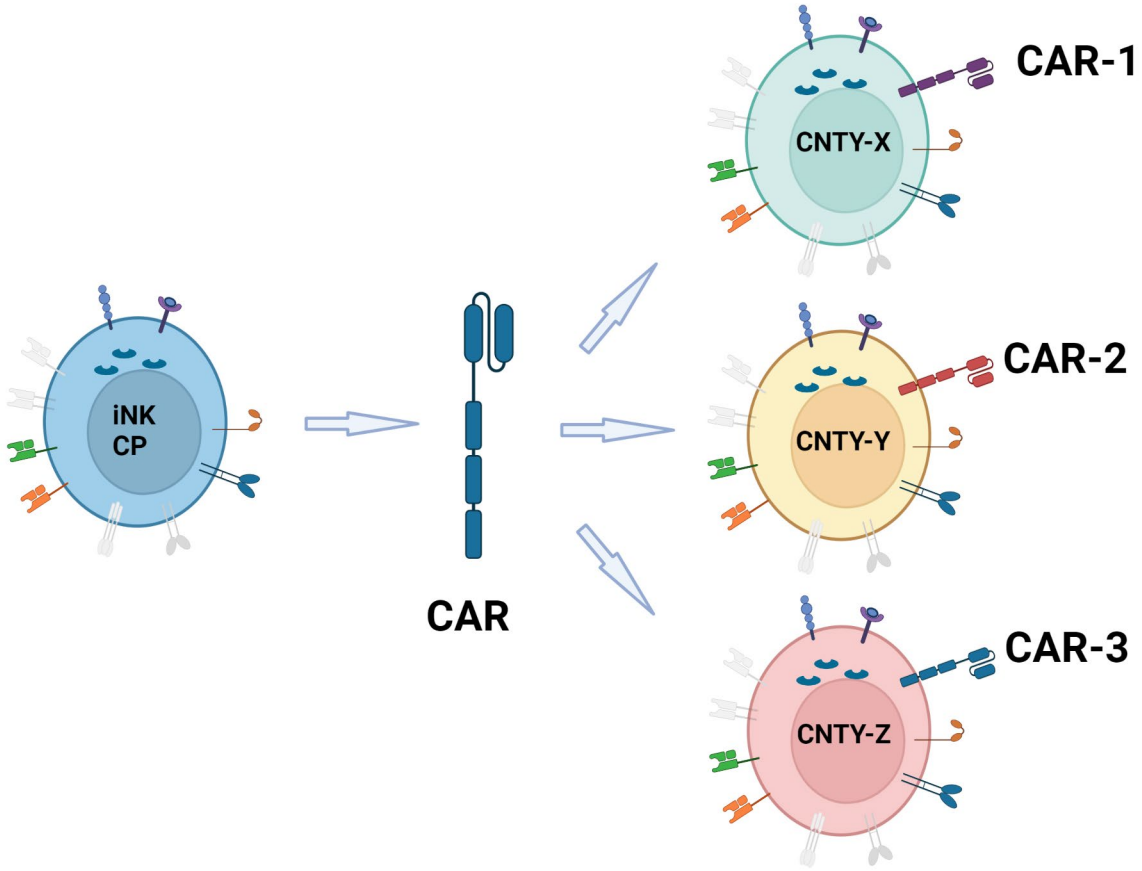
ENGINEERING PROFILE			
Step	**Gene Edit**		**Rationale**
1	KO	**NKG2A**	Potential to block inhibitory signal
	KI	**IL15/IL15Ra**	Homeostatic cytokine support
2	KO	B2M	Allo-Evasion
	KI	HLA-E-2A-**HLA-G**	Allo-Evasion
3	KO	CIITA ex5	Allo-Evasion
	KI	**HSV-TK-2A-PSMA**	Safety switch + cell tracer
4	KO	**CD70**	Landing pad, potential to enhance cell fitness
	KI	**CD16-2A-NKG2D**	Ab targeting + Tumor stress ligands
5	INS	CLYBL	Safe harbor site
	KI	CD133-CAR	Tumor targeting

Common Progenitor Features

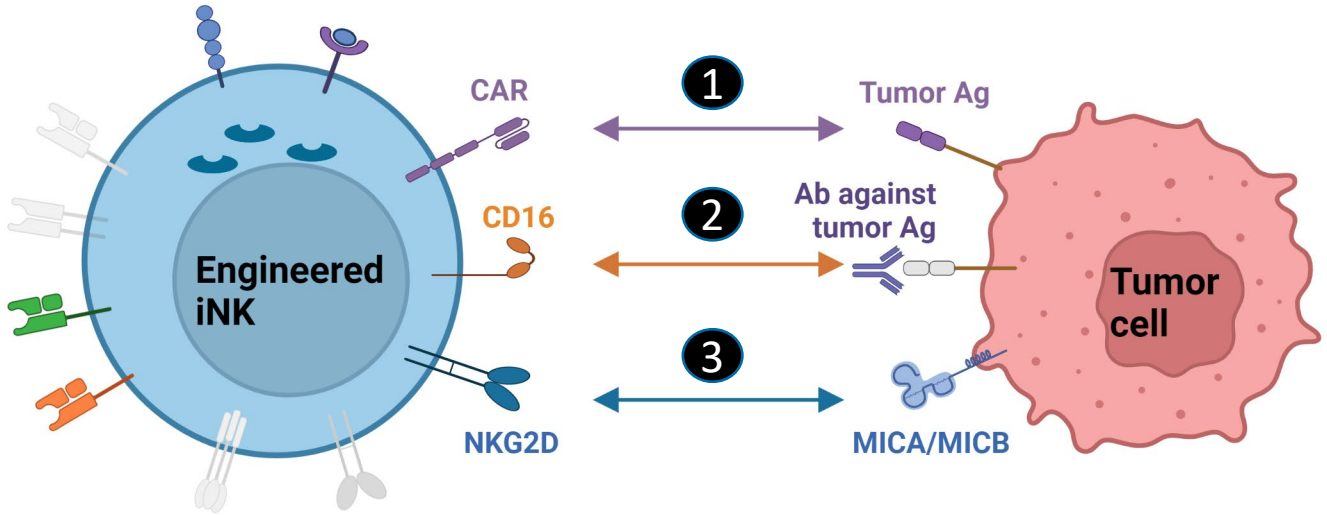
Boldface: iNK 3.0-specific gene edits

The iPSC Common Progenitor Enables Significant Cost and Time Efficiencies

One Common Progenitor → **Different CARs** → **Multiple Product Candidates**



iNK 3.0 Cell Platform Has Multiple Built-In Mechanisms for Tumor Cell Killing



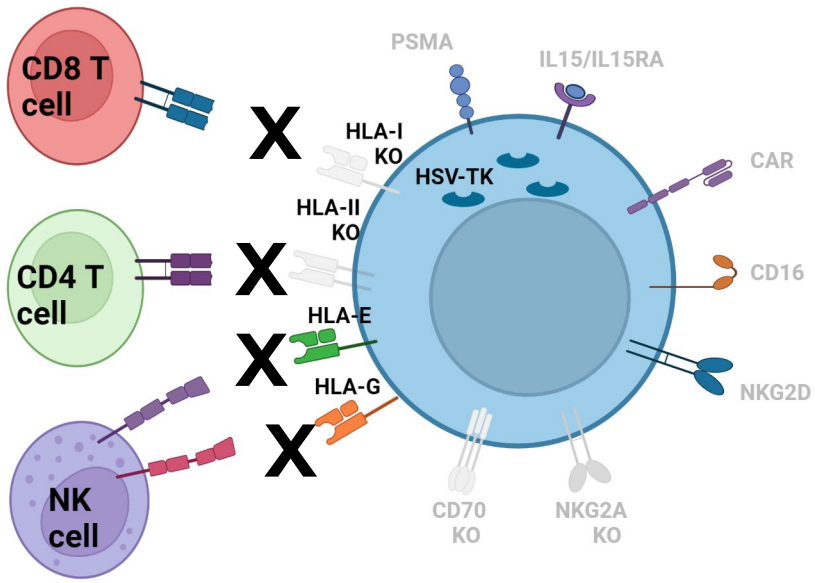
PATHWAYS FOR TUMOR KILLING

1. CAR-mediated killing
2. ADCC (Antibody-dependent cellular cytotoxicity)
3. NKG2D-mediated killing though recognition of stress ligands

iNK 3.0 Enhanced Allo-Evasion Features

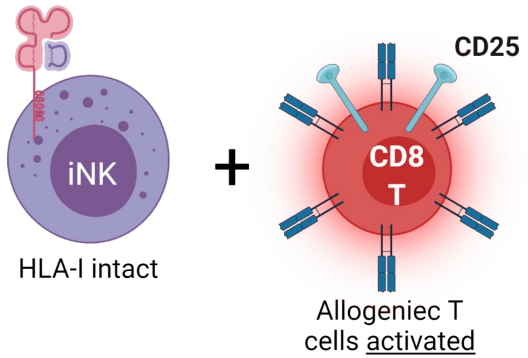
Allo-Evasion 3.0

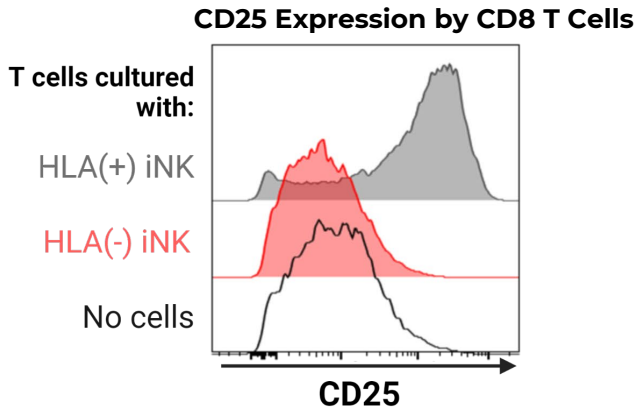
- Deletion of β2M designed to eliminate HLA-I expression and prevents recognition by CD8 T cells
- Knock out of CIITA designed to eliminate HLA-II expression and prevents recognition by CD4 T cells
- Knock-in of HLA-E and HLA-G prevent killing by NK cells

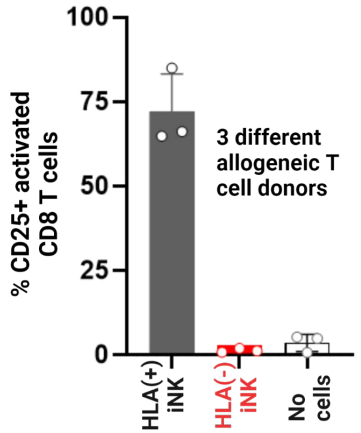


iNK Cells Lacking HLA-I Are Not Recognized by Allogeneic CD8 T cells

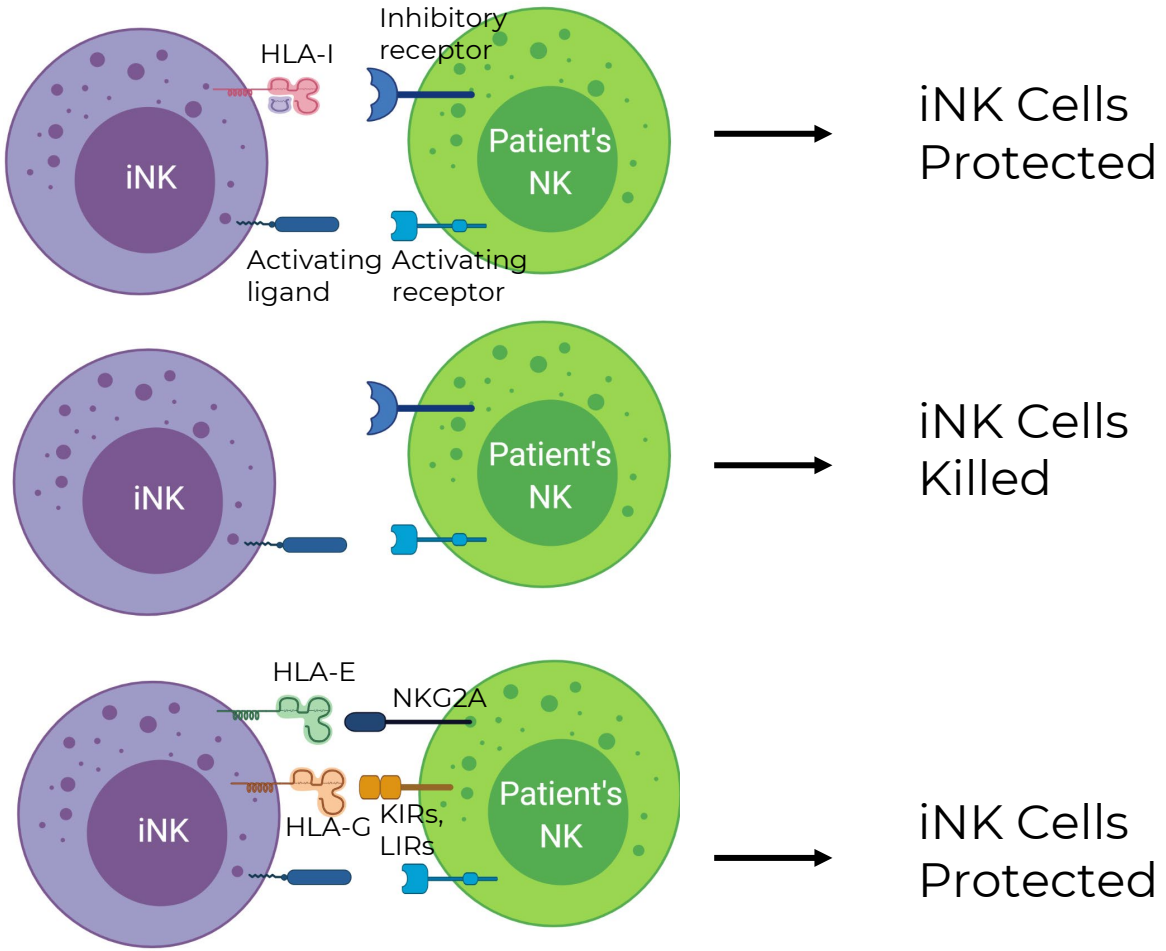
iNK Cells Expressing HLA-I Cause Allogeneic CD8 T Cell Activation, But Not HLA-I Null iNK Cells





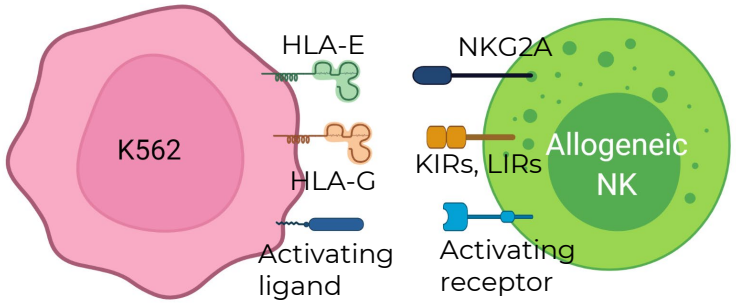


Lack of HLA-I on iNK Cells Can Lead to Their Elimination by Allogeneic NK Cells



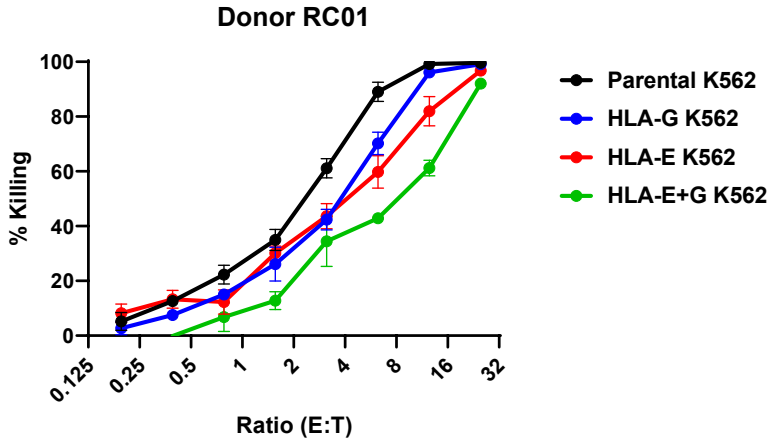
Expression of HLA-E + HLA-G Offers Better Protection From NK Cell Killing

Proof-of-Concept Study with HLA-I Null K562 Cells Engineered with HLA-E and HLA-G

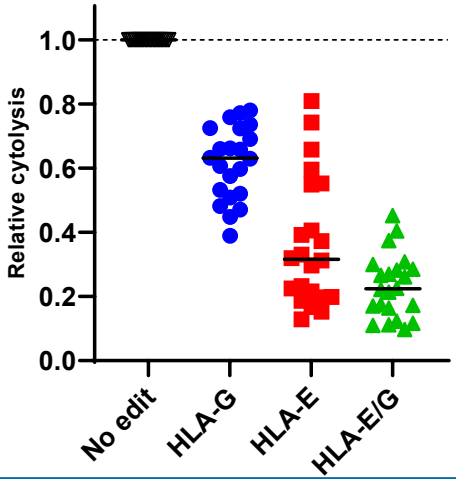


- HLA-E and HLA-G engage different receptors on NK cells including NKG2A, KIRs, and LIRs
- The expression of NKG2A, KIRs, and LIRs varies among NK cells from different donors

The Combination of HLA-E + HLA-G Improved Protection to Killing by Allogeneic NK Cells

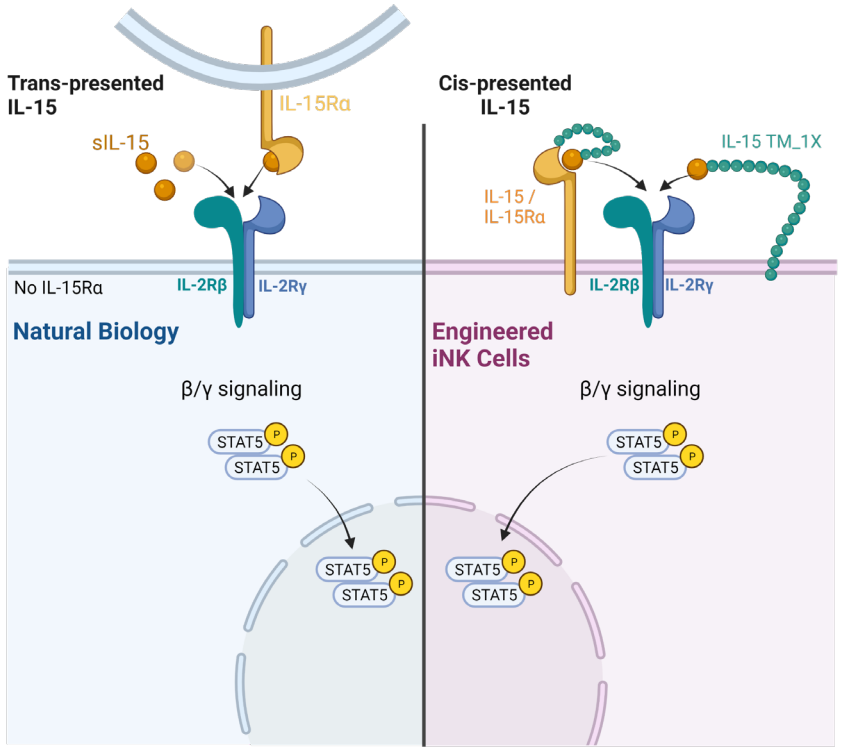


Agglomerated Data from 22 NK Cell Donors

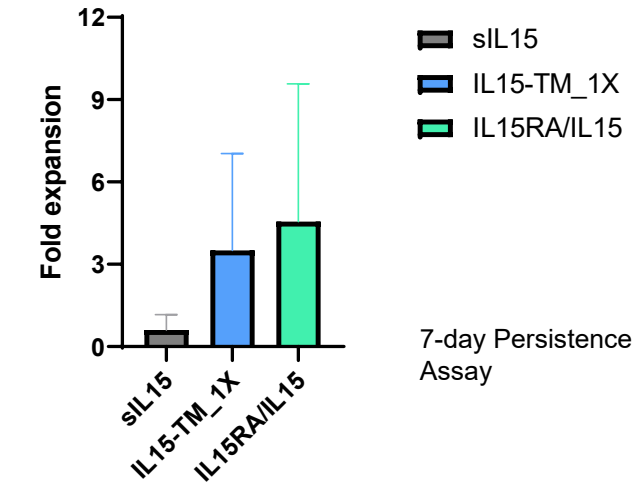


Membrane-Bound IL-15/IL-15RA Enhances iNK Cell Persistence in vitro

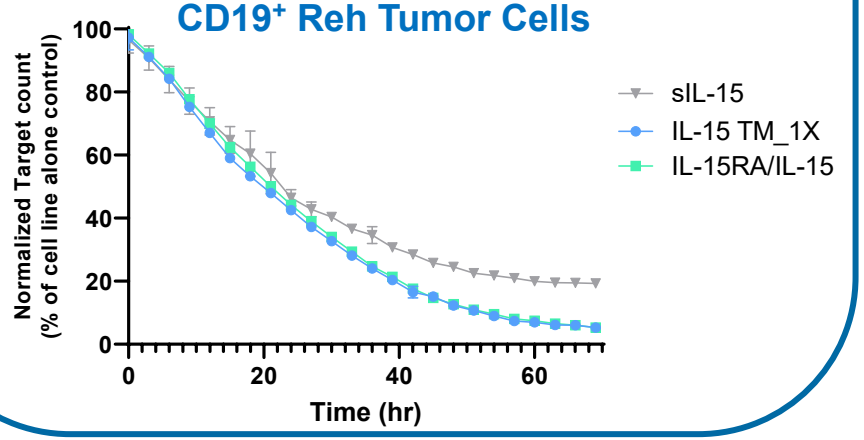
IL-15 Receptor Engagement and Signaling



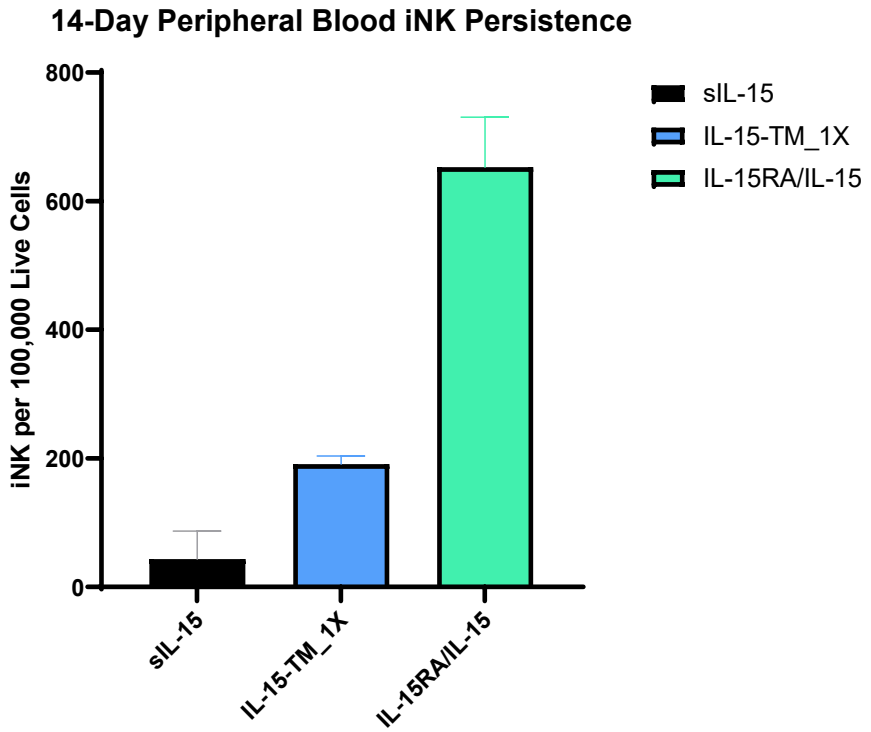
Membrane-bound IL-15 Improves iNK Cell Persistence In Vitro

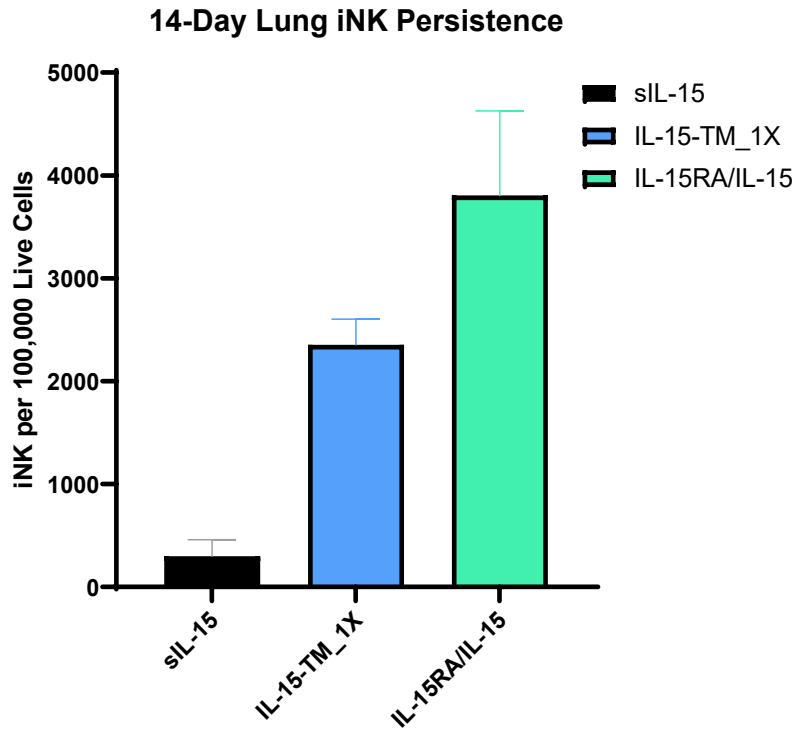


Membrane-bound IL-15 Improves Killing CD19⁺ Reh Tumor Cells

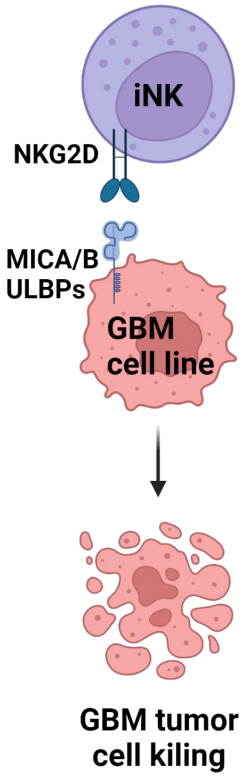


Engineered IL-15/IL-15RA Enhances iNK Cell Persistence in vivo

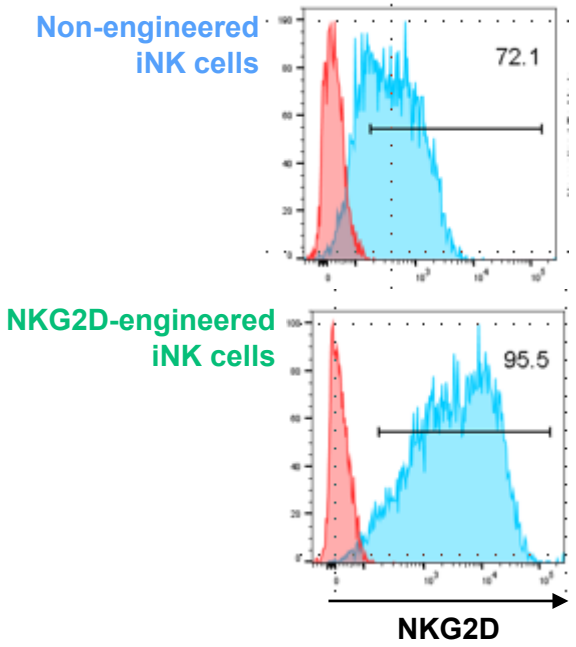




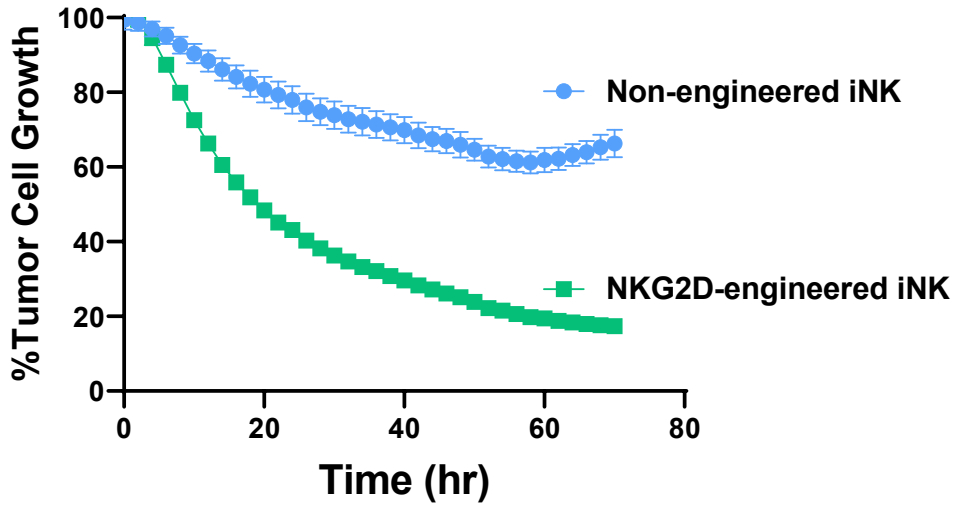
Engineered NKG2D Expression on iNK Cells Enhances Tumor Killing



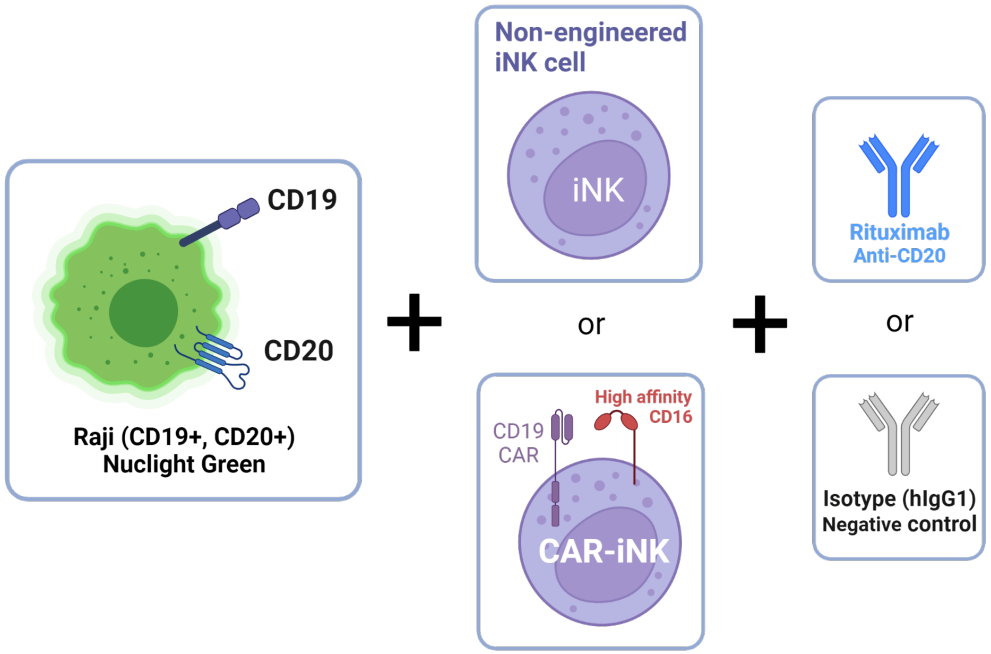
Engineered iNK Cells Express Higher Levels of NKG2D



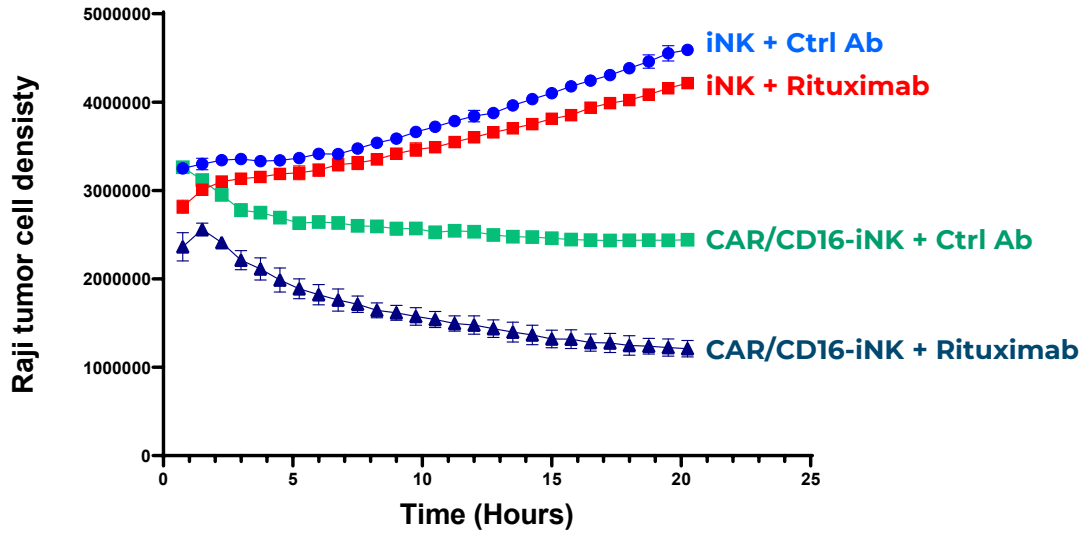
NKG2D-Engineered iNK Cells Mediate Robust Killing of the U87 GMB Cell Line



High-affinity CD16 Augments CAR-Mediated Killing of Tumor Cells Through Antibody-Dependent Cellular Cytotoxicity (ADCC)



iNK Cells Engineered with High Affinity CD16 Mediate Robust ADCC of Tumor cells



Pivoting to the iNK 3.0 Platform to Create Next-Gen CNTY-103 Is Expected to Improve the Likelihood of Clinical Success

The iNK 3.0 Platform incorporates multiple features that are highly relevant for the treatment of GBM

Pivoting to the iNK 3.0 platform is expected to improve the likelihood of clinical success for CNTY-103 without a major timeline impact

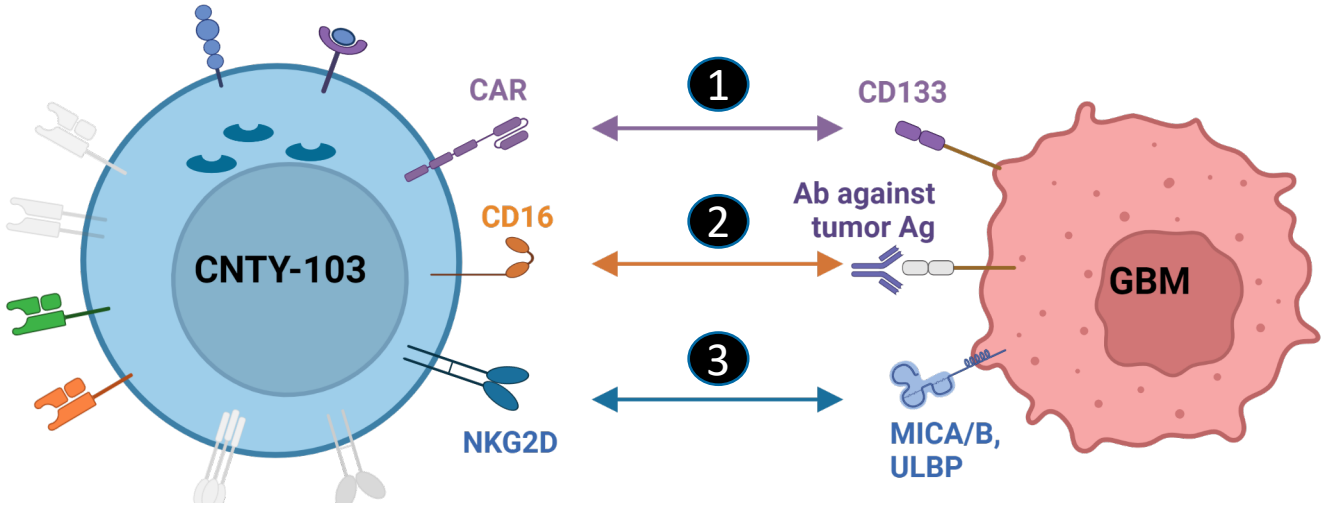
Next-Gen CNTY-103 uses a single specificity CAR to target CD133 and adds two additional mechanisms for tumor cell killing (NKG2D and CD16)

- Targeting of EGFR is leveraged through the combination with an anti-EGFR antibody that acts through CD16

PET-reporter (PSMA) provides a non-invasive image tool that we believe will help gain significant insights on the persistence and migration of CNTY-103 iNK cells after infusion

The incorporation of a safety switch is expected to improve the safety profile

Next-Gen CNTY-103 Has Multiple Built-in Mechanisms for Enhanced Anti-tumor Activity



MULTIPLE MECHANISMS TO CONTROL TUMOR GROWTH

Tumor Killing

1. CD133 CAR-mediated tumor cell killing
2. CD16-mediated killing using Abs against tumor antigens (EGFR, HER2, CD70, others)
3. NKG2D-mediated killing though recognition of stress ligands (MICA/B, ULBPs)

Tumor Microenvironment Modulation

- Elimination of suppressive cells within TME using Abs (CD73, CSF1R, PD-L1, others)

CENTURY
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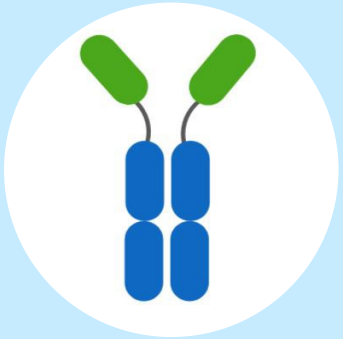
Century's Novel Universal Targeting Receptor Adaptor Platform

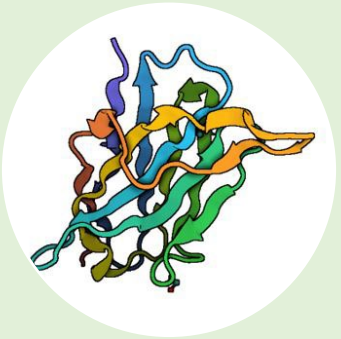
Jill Carton, PhD I Executive Director of CAR Engineering and Protein Sciences

Century's Protein Sciences Capabilities Drive Sophisticated Therapeutic Solutions



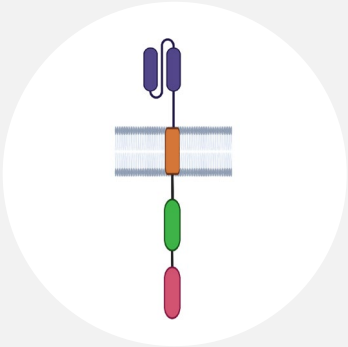
Antibody Discovery

Century Therapeutics' proprietary Phage Display Library for novel humanized VHH tumor target binders



Protein Biochemistry

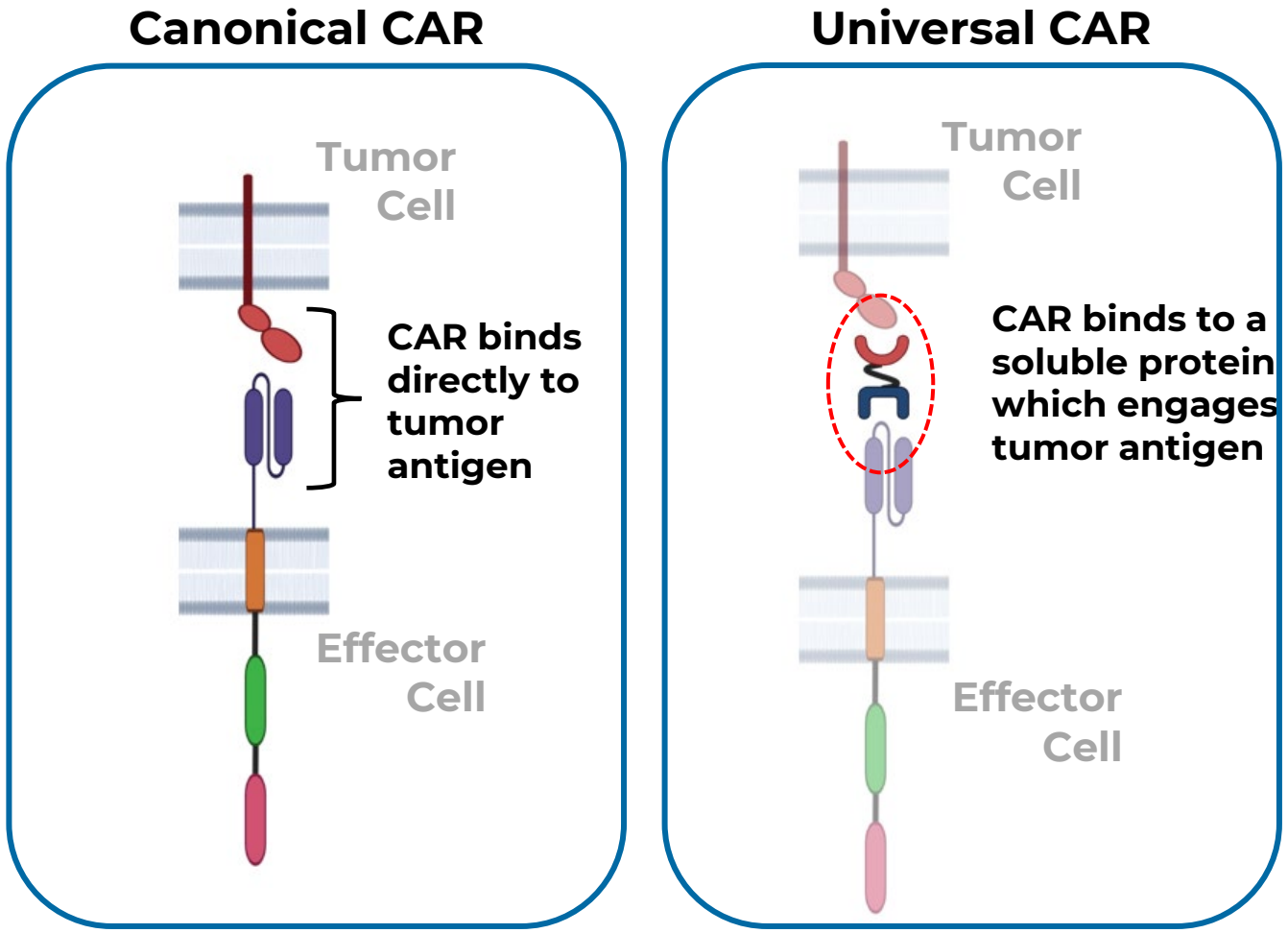
Protein stability and biophysical characteristics designed to produce safe and consistent products



Protein Engineering

Fit-for-purpose CAR assembly and transgene designs for therapeutic cell features, allo-evasion, safety switch, cytokines

Universal CAR Platforms Extend the Versatility of Conventional CARs



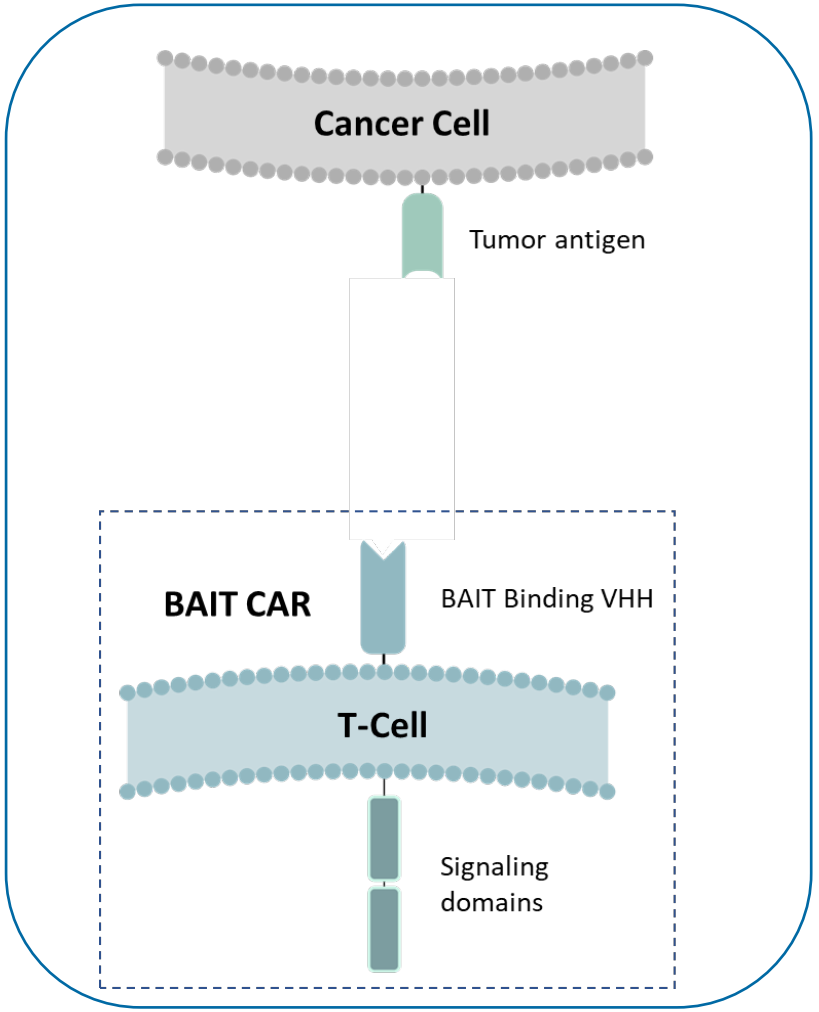
Universal CAR has two components:

1. CAR that binds a tag on a soluble protein
2. Soluble protein that binds to the tumor cell antigen and the CAR

Effector cell mediated tumor cell killing is only activated when the soluble protein engages both the CAR and the tumor antigen

Activity of the CAR can be modulated by the tumor targeting specificity and dose of the soluble protein

Century's Novel Universal Targeting Receptor Adaptor Platform (uTRAP) is Versatile and Flexible

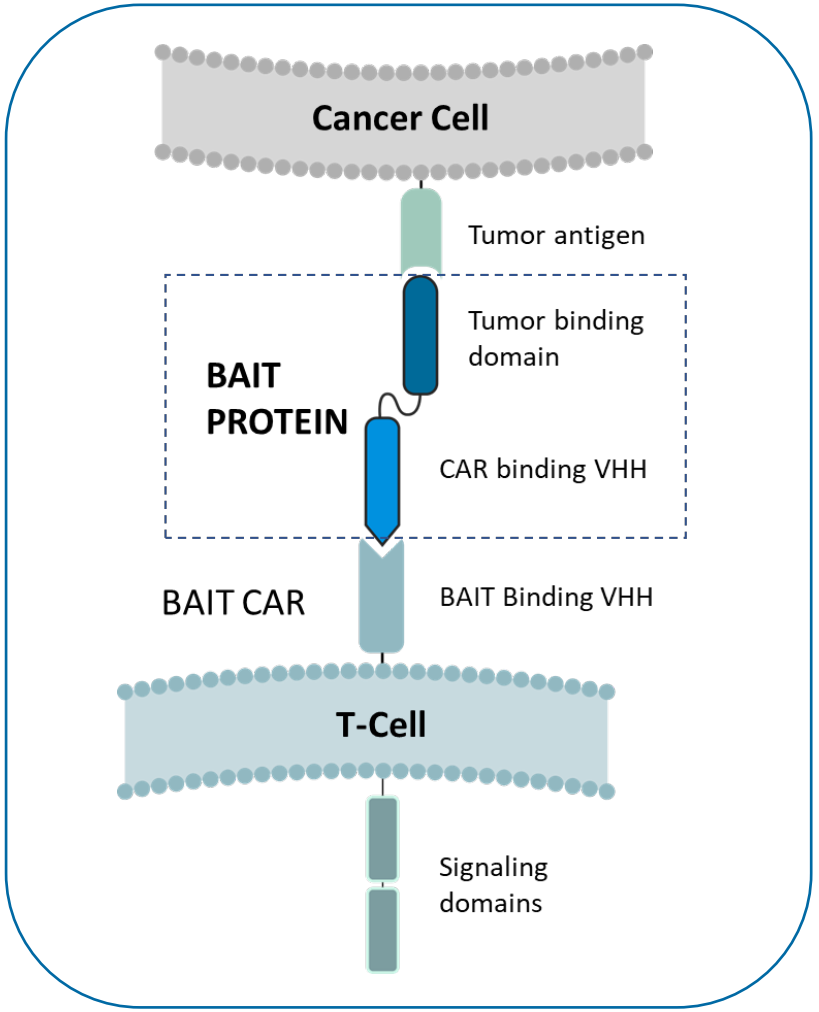


uTRAP is built on highly adaptable, single domain VHH proteins

1. **BAIT CAR**

- Inactive in circulation
- Inactive in the presence of tumor cells

Century's Novel Universal Targeting Receptor Adaptor Platform (uTRAP) is Versatile and Flexible



uTRAP is built on highly adaptable, single domain VHH proteins

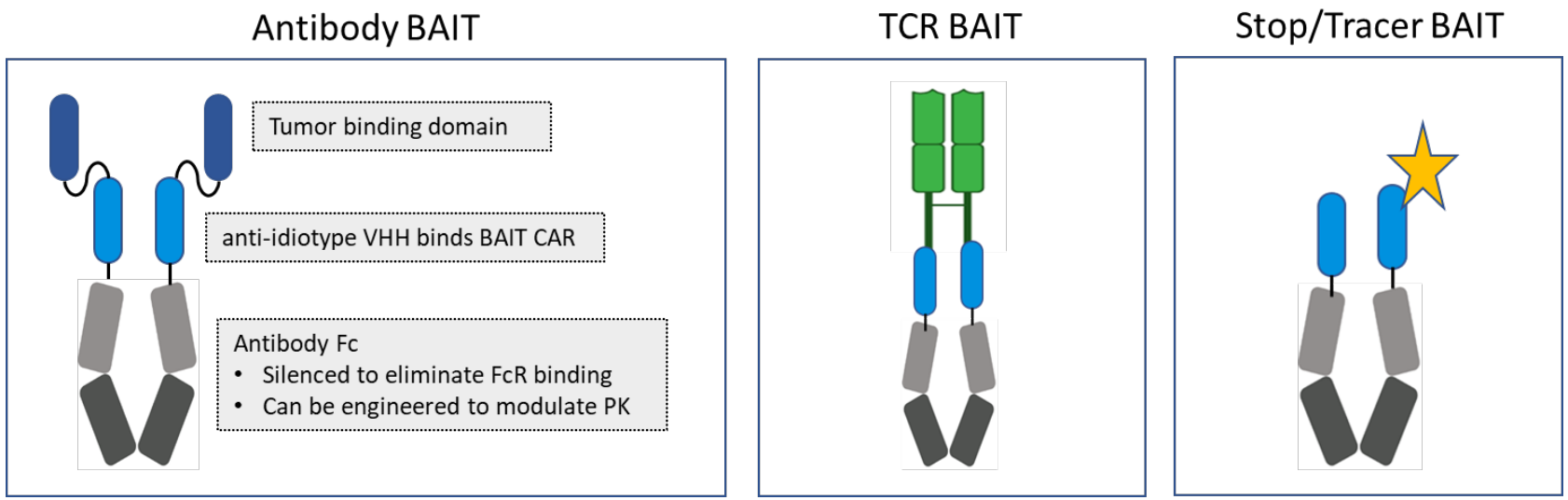
1. BAIT CAR

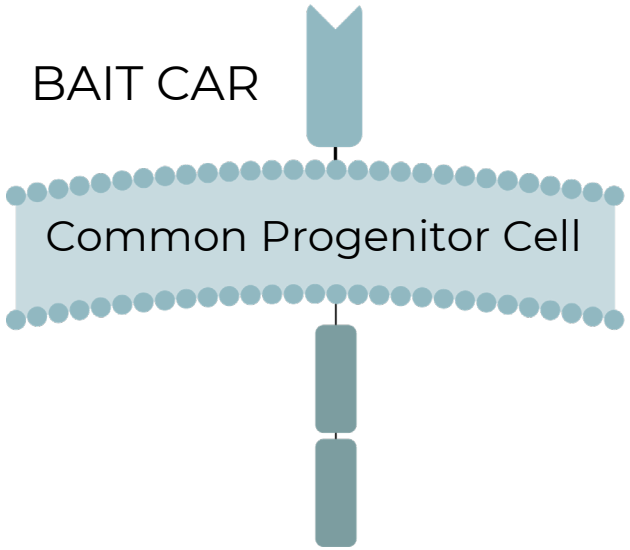
- Inactive in circulation
- Inactive in the presence of tumor cells

2. Bispecific Anti-Idiotype Targeting (BAIT) Protein

- Exploits the high specificity of an anti-Idiotype antibody
- Adaptable binding affinity to the CAR and to the tumor antigen
- Effector cell mediated tumor cell killing is only activated when the BAIT engages both the CAR and the tumor antigen

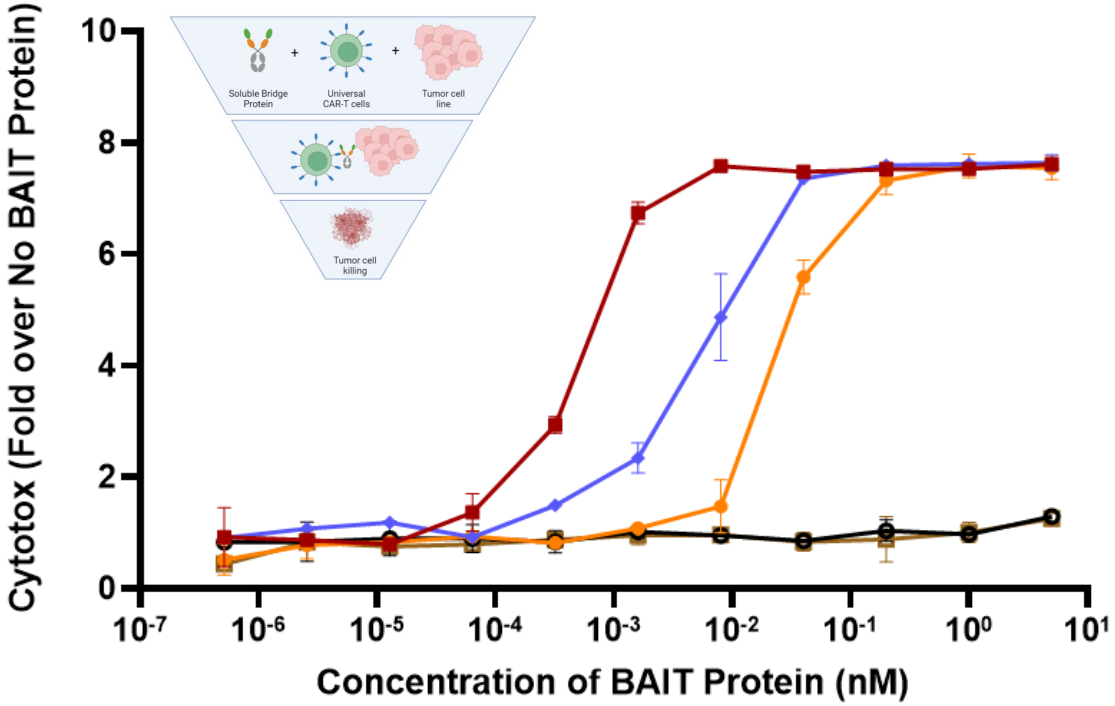
BAIT Proteins are Engineered for Diverse Functions and Used With a Single Cell Line

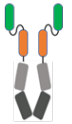
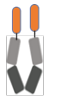




Century's uTRAP Platform Mediates Potent Cytotoxicity

In Vitro Killing of NALM6 EGFR+ Cells through uTRAP engineered T-Cells In the presence of EGFR BAIT proteins

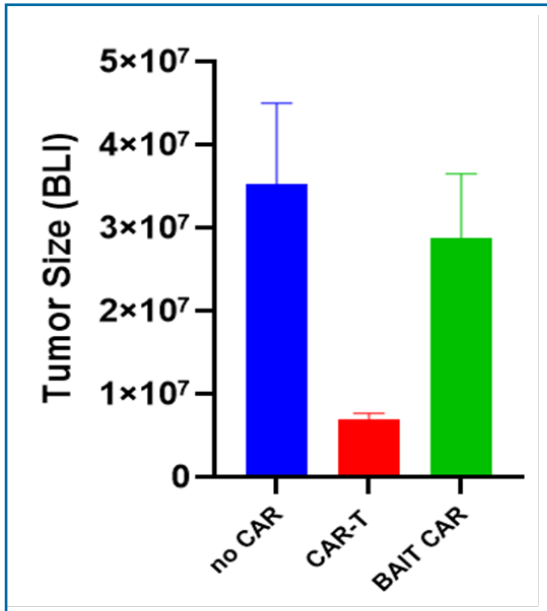


Sample	Format	EC50 (pM)
BAIT 1		0.5
BAIT 2		5.1
BAIT 3		22.3
BAIT 4		CAR only binder
BAIT 5		Tumor only binder

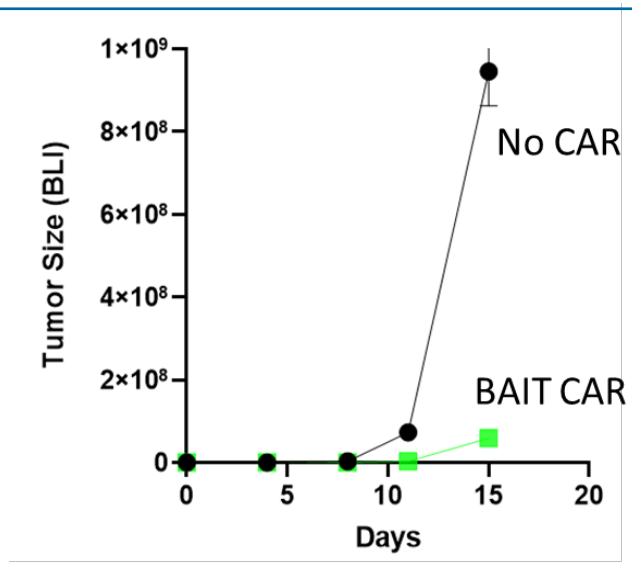
BAIT protein engineering can modulate functionality

In vivo Proof of Concept Studies with Century's uTRAP Platform Initiated

In vivo studies with Peripheral Blood T-cells

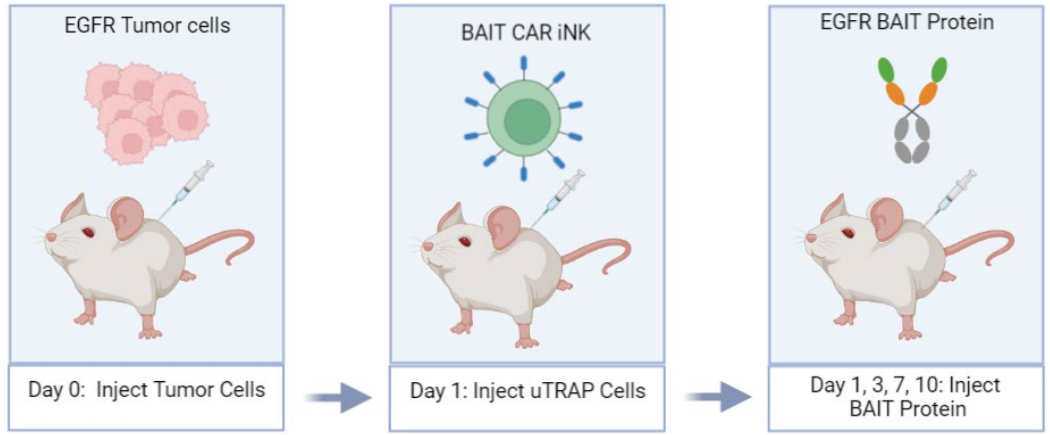


BAIT CAR-T cells are inert without Bridge Protein



BAIT CAR-T cells are potent killers on Ag+ cells

uTRAP in vivo efficacy studies in IPSC-derived iNK and iT cells are initiated

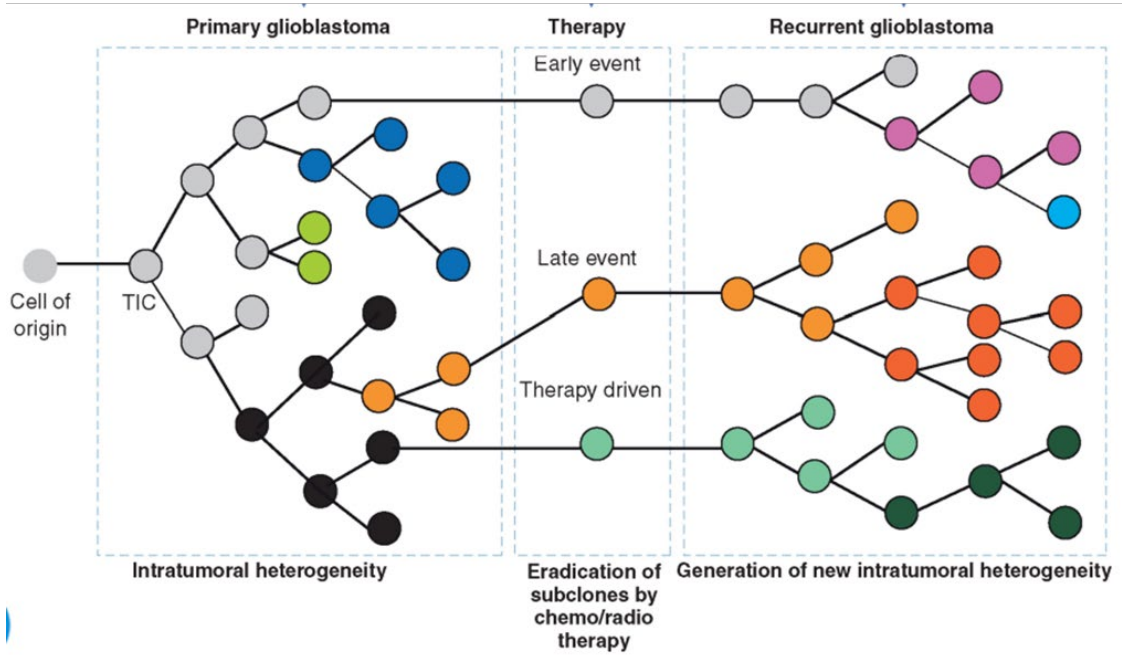


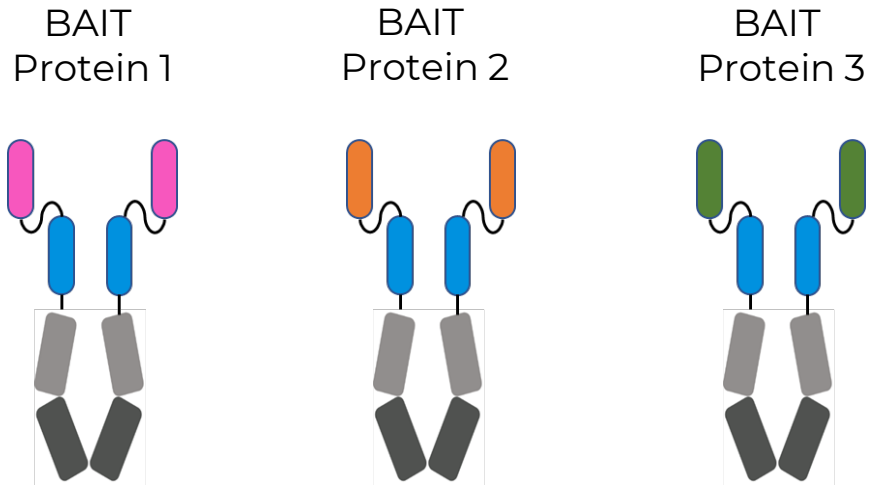
Century's uTRAP Addresses Multiple Clinical Challenges

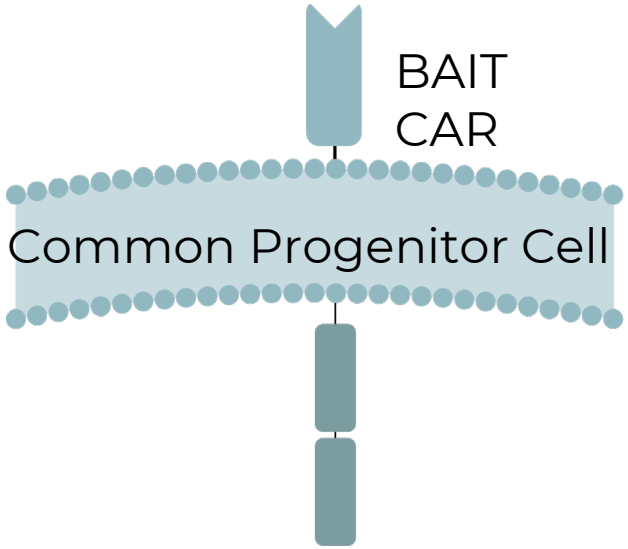
Advantage	
Extend the target landscape	Tunable potency and temporal regulation of BAIT protein increases control of target engagement Antibody and TCR BAIT formats access cell surface and intracellular targets
Address tumor heterogeneity	Soluble BAIT proteins can target multiple antigens, each for use with a single uTRAP cell line One cell line can be used to develop many therapeutic approaches
Widen the therapeutic window	Tunable potency and temporal regulation of activity provides greater control over adverse effects
On/Off safety switch	Soluble protein half-life regulation allows for off-switch Stop or Eliminate BAIT proteins can switch off/clear uTRAP cells
Tracking and detecting	Non-targeted, labelled BAIT protein to trace engineered cells

uTRAP Enables a Therapeutic Strategy to Tackle Tumor Heterogeneity in Glioblastoma

Evolution of GBM tumor target profile







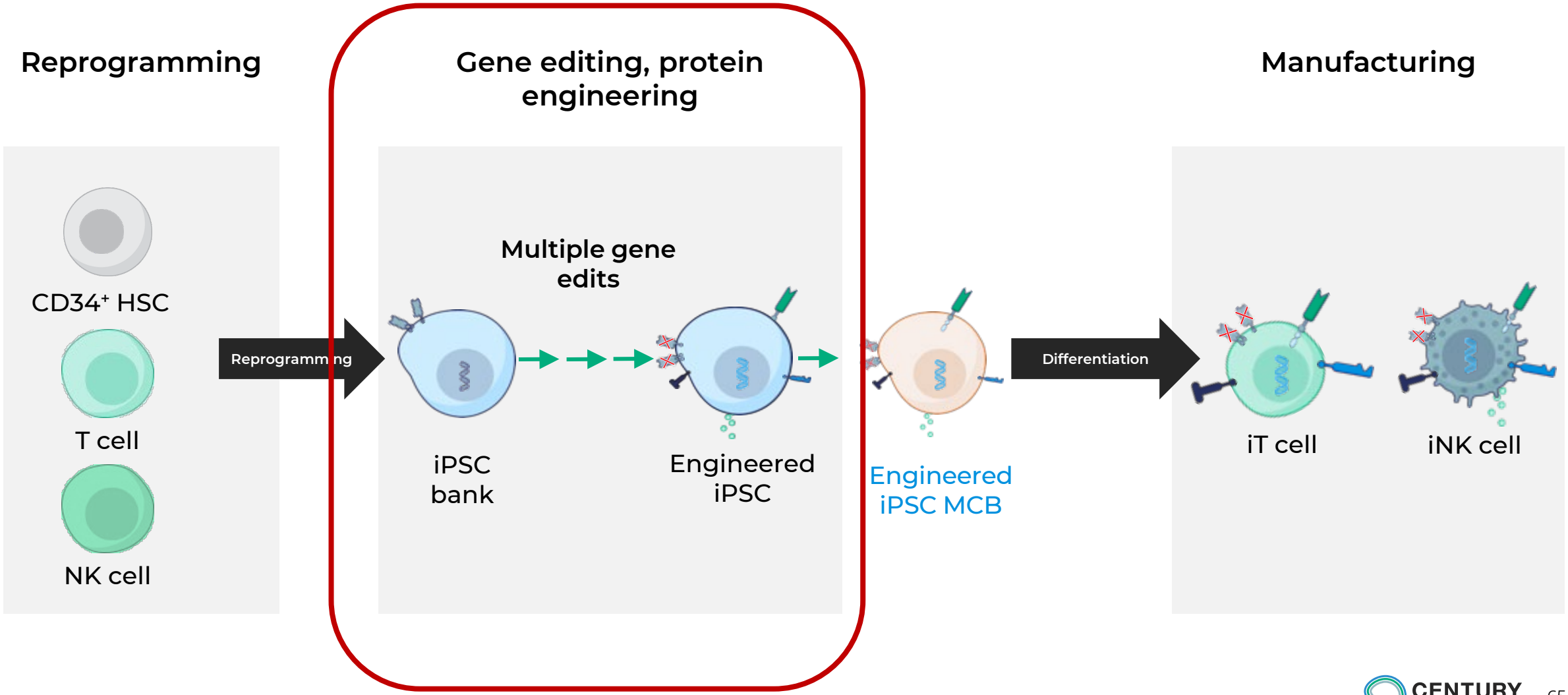
CENTURY THERAPEUTICS

CENTURY THERAPEUTICS

MAD7 CRISPR Nuclease for iPSC Genome Engineering

Michael Naso, PhD I VP Cell Engineering

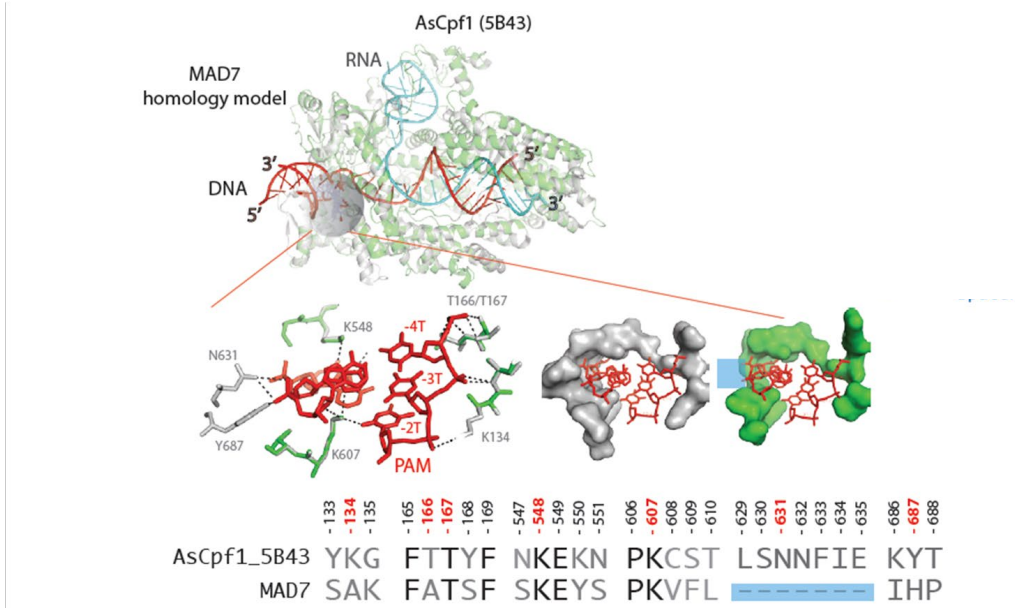
Century's End-to-End Platform Has the Key Components to Realize Potential of iPSC

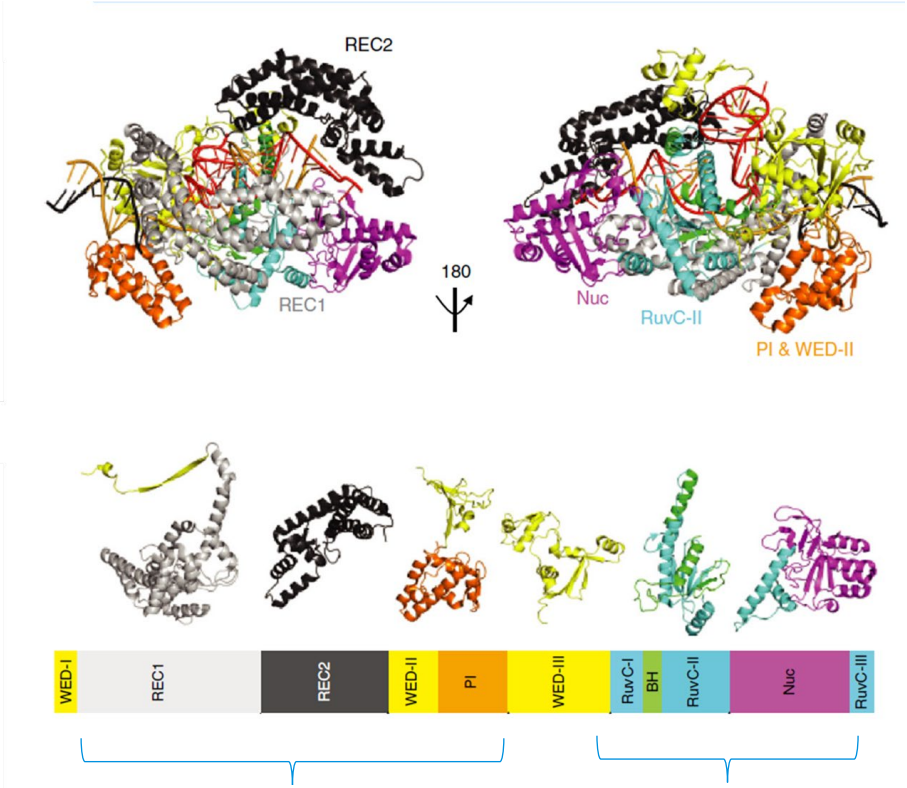


Product Candidate Engineering Requires a High Functioning and Reliably Sourced CRISPR Nuclease

Attribute	Preference for product candidate engineering
Double-stranded gDNA cleavage	High efficiency in iPSCs
Fidelity	Low off-target cutting
Gene insertion	High efficiency HDR in iPSCs
PAM site recognition	Prevalent throughout genome
Delivery	RNP formulation
Regulatory compliance	Complete documentation for all components

MAD7 is a Novel Class 2 Type V-A CRISPR Nuclease





Target DNA recognition

Target DNA cleavage

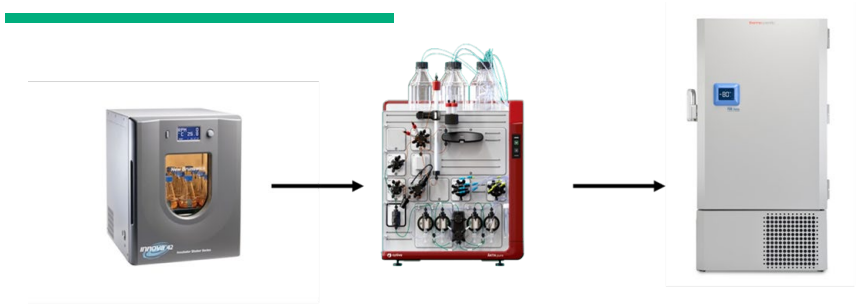
High structural homology to Cpf1 (Cas12a), low sequence identity (~30%)

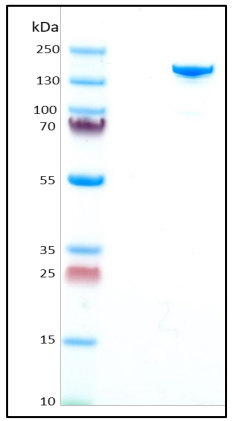
T-rich PAM site similar to Cpf1

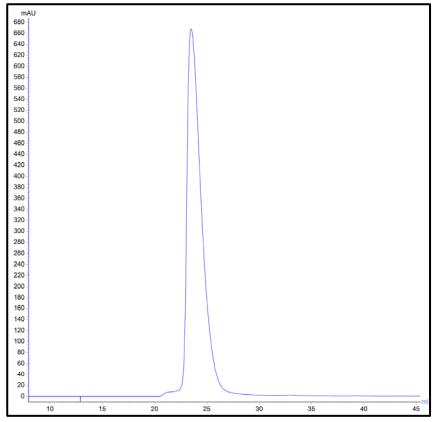
Single molecule gRNA

Staggered DNA cutting to facilitate HDR

MAD7 Produced in House In E. Coli and is Functionally Equivalent to Industry Standard Cpf1







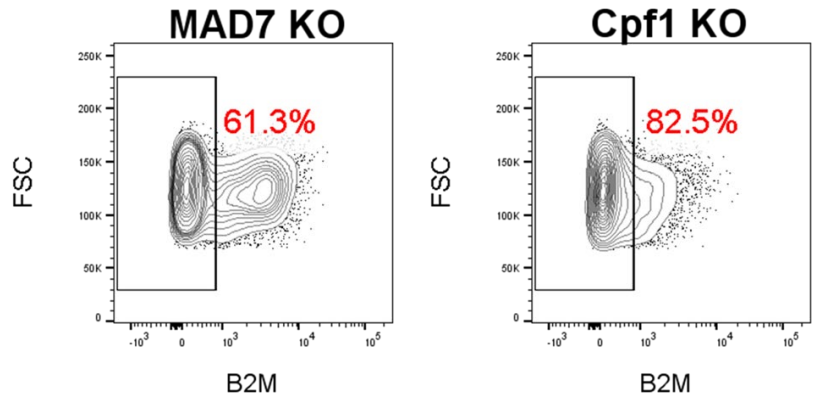
Multi-step column purification yields homogenous MAD7 protein

MAD7 RNPs function comparably to Cpf1 in iPSCs

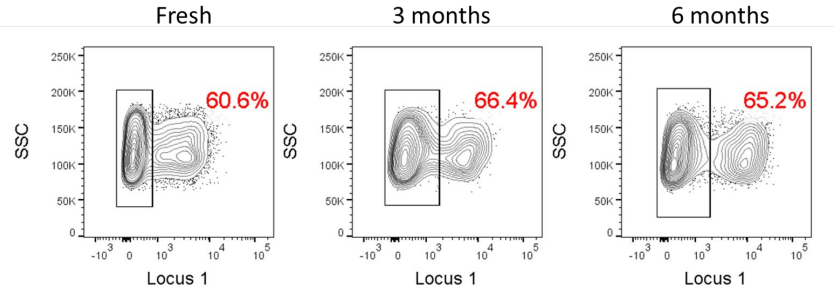
MAD7 protein is stable for at least 6 months at -80C

Regulatory compliant production process

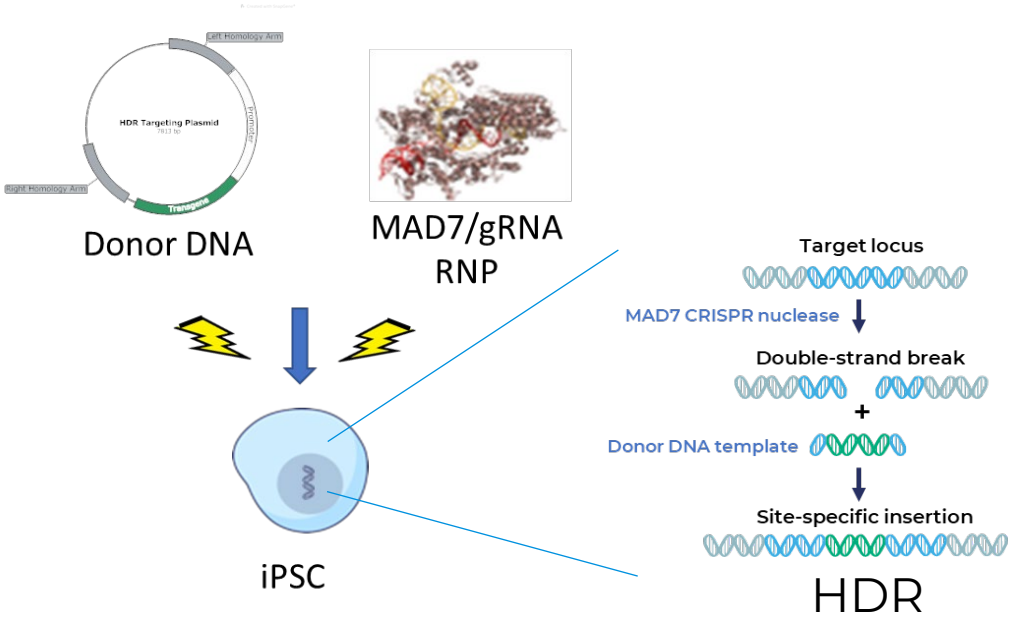
Knock-out efficiency of MAD7 is as efficient as Cpf1



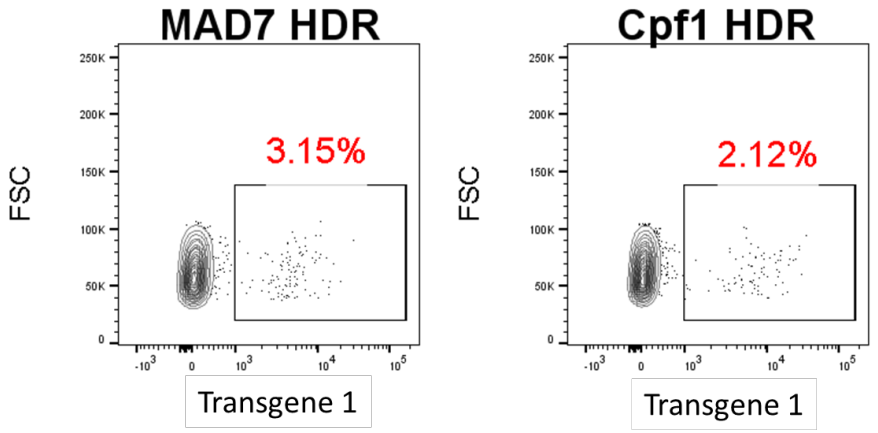
Purified MAD7 activity is maintained for >6 months at -80C



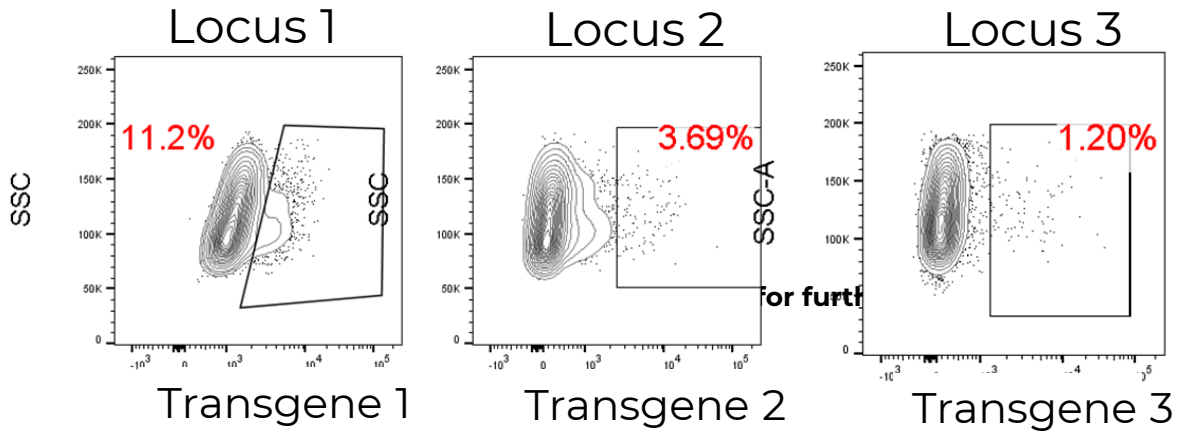
Mad7 Facilitates HDR at Multiple Loci in iPSCs at Efficiencies Seen with Cpf1



HDR efficiency with MAD7 is equivelent to Cpf1

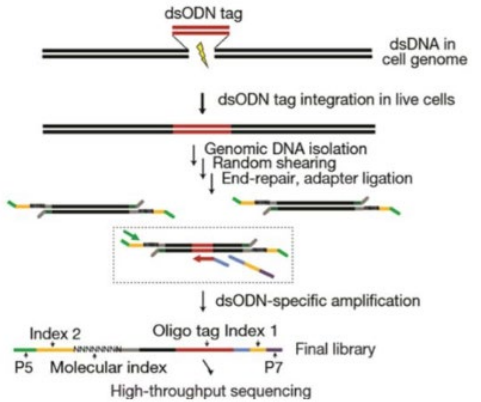


High HDR efficiency with MAD7 at multiple loci



MAD7 is a High-Fidelity CRISPR Nuclease with Off-Target Rates at Least as Good as Cpf1

Guide-seq off-target analysis



On-target Basic

Sample	BED Chromosome	Position	Total Reads	+Reads	-Reads	+ODN Reads	-ODN Reads
B2M	chr15	44715402	56233	21227	35006	31331	19947

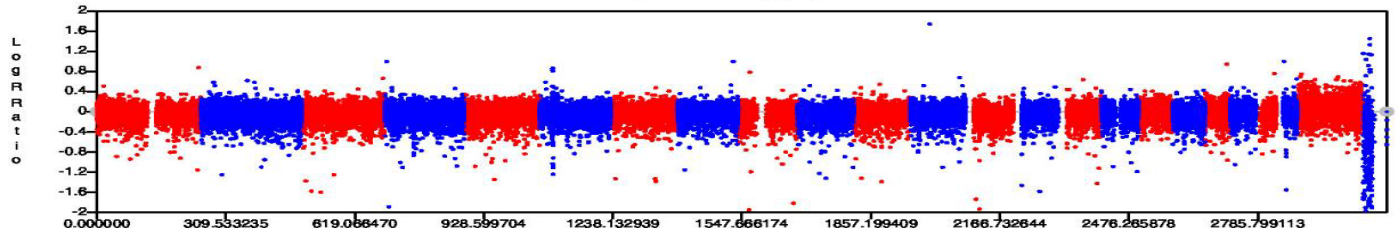
Off-target Basic

Sample	BED Chromosome	Position	Total Reads	+Reads	-Reads	+ODN Reads	-ODN Reads
B2M	chr11	58181531	192	0	192	2	168
	chr10	22976139	72	72	0	3	68

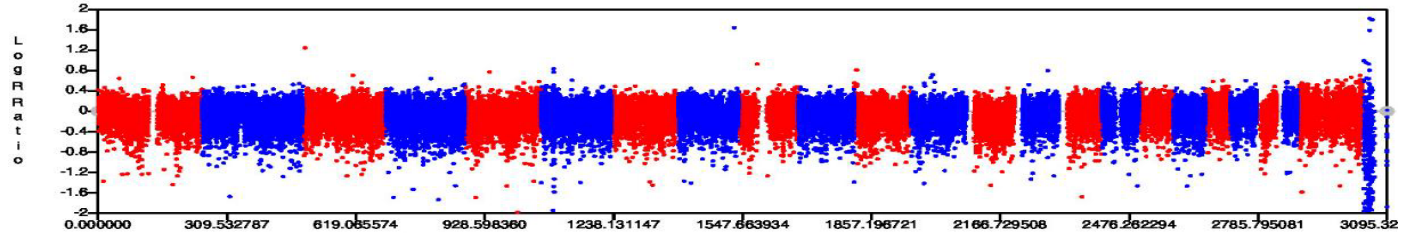
Guide-seq characterization revealed very low frequency of off-target cutting, comparable to Cpf1, in iPSCs

SNP CNV array analysis

iPSC donor line



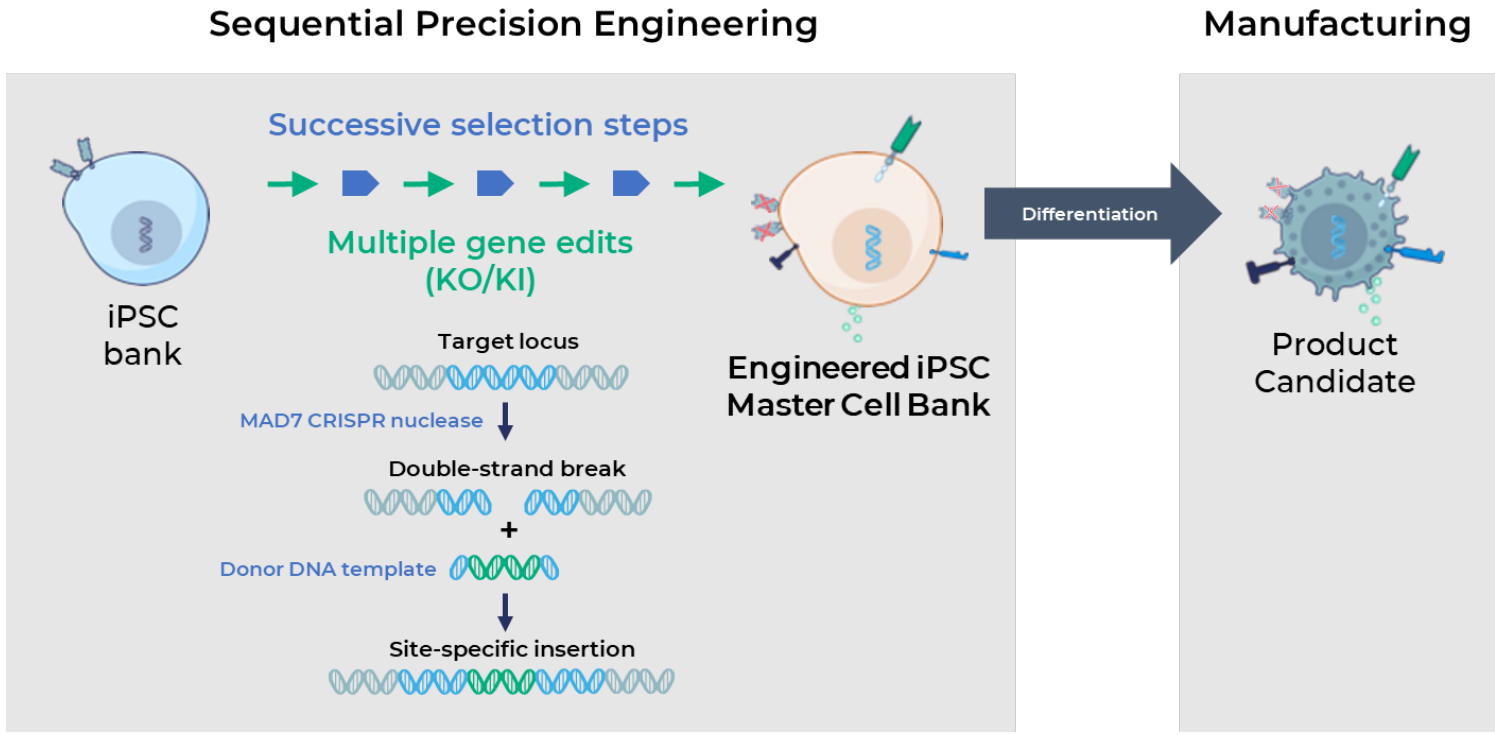
Engineered iPSC donor line



- SNP microarray CNV analysis does not show increased frequency of small or large CNVs with MAD7, comparable to Cpf1, in iPSCs

WGS performed on all lead single-cell clones to confirm fidelity

We Have Pivoted to MAD-7 for Platform and Pipeline Engineering of All Product Candidates



No impact on viability or pluripotency after multiple uses of MAD7 in iPSCs

Process used to make common progenitor iPSC clone for CAR insertion to support multiple programs

We Continue to Optimize and Evolve Our Mad7 Platform

Increasing protein production yield and long-term stability

PAM site evolution

Increased HDR efficiencies with further protein engineering

MAD7-on and MAD7-off fusions for gene regulation strategies

CENTURY THERAPEUTICS

Concluding Remarks

Lalo Flores, PhD I CEO

CENTURY THERAPEUTICS

Emerging leader in allogeneic cell therapies for cancer

Comprehensive iPSC cell platform

With end-to-end capabilities to develop iNK and γδiT cell candidates

Disruptive, fit-for-purpose approach for GBM

CNTY-103 engineered with multiple features to increase PTS

Toolbox to address solid tumors

iNK 3.0 platform and γδiT cell platform engineered with versatile features like UTRAP

Emerging pipeline of candidates

Product engine anticipated to deliver 5 INDs over the next 3 years

Financial Strength

Cash runway into 2025
Ended 1Q22 with cash, cash equivalents, and investments of $466.4M

CENTURY THERAPEUTICS

Q&A

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Thank you