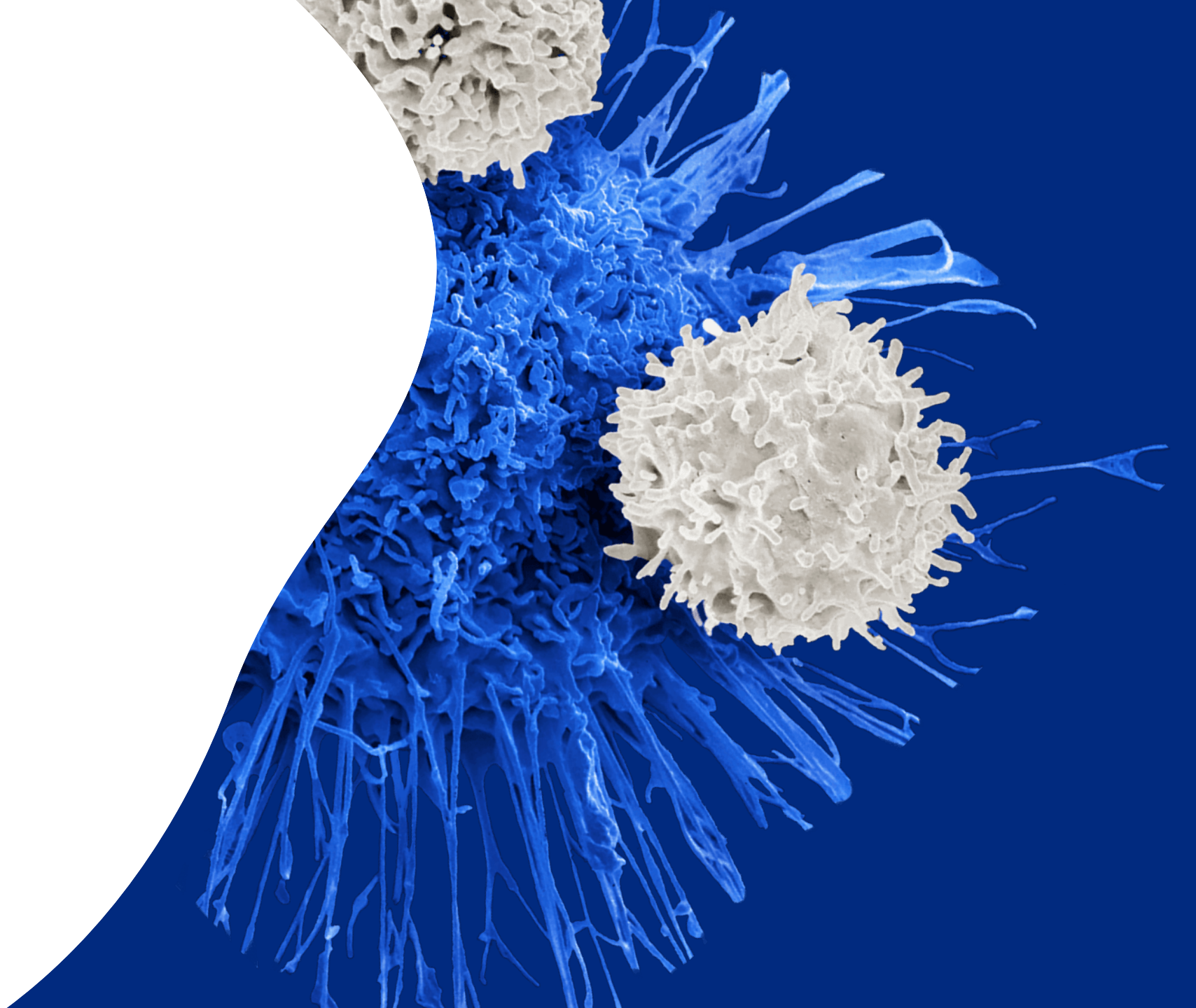
CENTURY THERAPEUTICS

R&D Day

November 11, 2022



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Agenda

Delivering on a Next-Generation iPSC Platform

Lalo Flores, PhD, CEO

Nectin-4 directed therapies: Urothelial Cancer and Beyond

Jonathan Rosenberg, MD, Chief Genitourinary Oncology Service, Division of Solid Tumor Oncology; Enno W. Ercklentz Chair, Memorial Sloan Kettering Cancer Center

Rationale for iPSC-derived γδ CAR-T cells

Hy Levitsky, MD, President of Research & Development

Century's Gamma Delta iT Cell Platform

Mark Wallet, PhD, Vice President, Head of Immuno-Oncology

CNTY-107, our γδ iT Product Candidate for the Treatment of Solid Tumors Expressing Nectin-4

Luis Borges, PhD, CSO

Q&A

CENTURY
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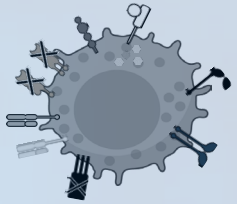
Delivering on a Next-Generation iPSC Platform

Lalo Flores, PhD I CEO

Positioned to Deliver Next-Generation Cell Therapies

First IND (CNTY-101) deemed eligible to proceed by FDA, Poised to initiate Phase 1 imminently



Advances with next generation iNK 3.0 and gamma delta iT cell platforms

Foundational investment to establish in-house manufacturing

Maintaining financial strength with cash runway into 2025

Century's Key Areas of Internal Focus

B cell malignancies

CNTY-101: Lead product candidate, CD19 targeted CAR-iNK

CNTY-102: First γδ iT candidate, multi-specific (CD19 + CD79b) CAR-iT

Designed to increase proportion of patients achieving durable responses through multi-dosing regimens enabled by key Allo-Evasion™ edits

Glioblastoma

CNTY-103: CD133 CAR iNK for recurrent GBM

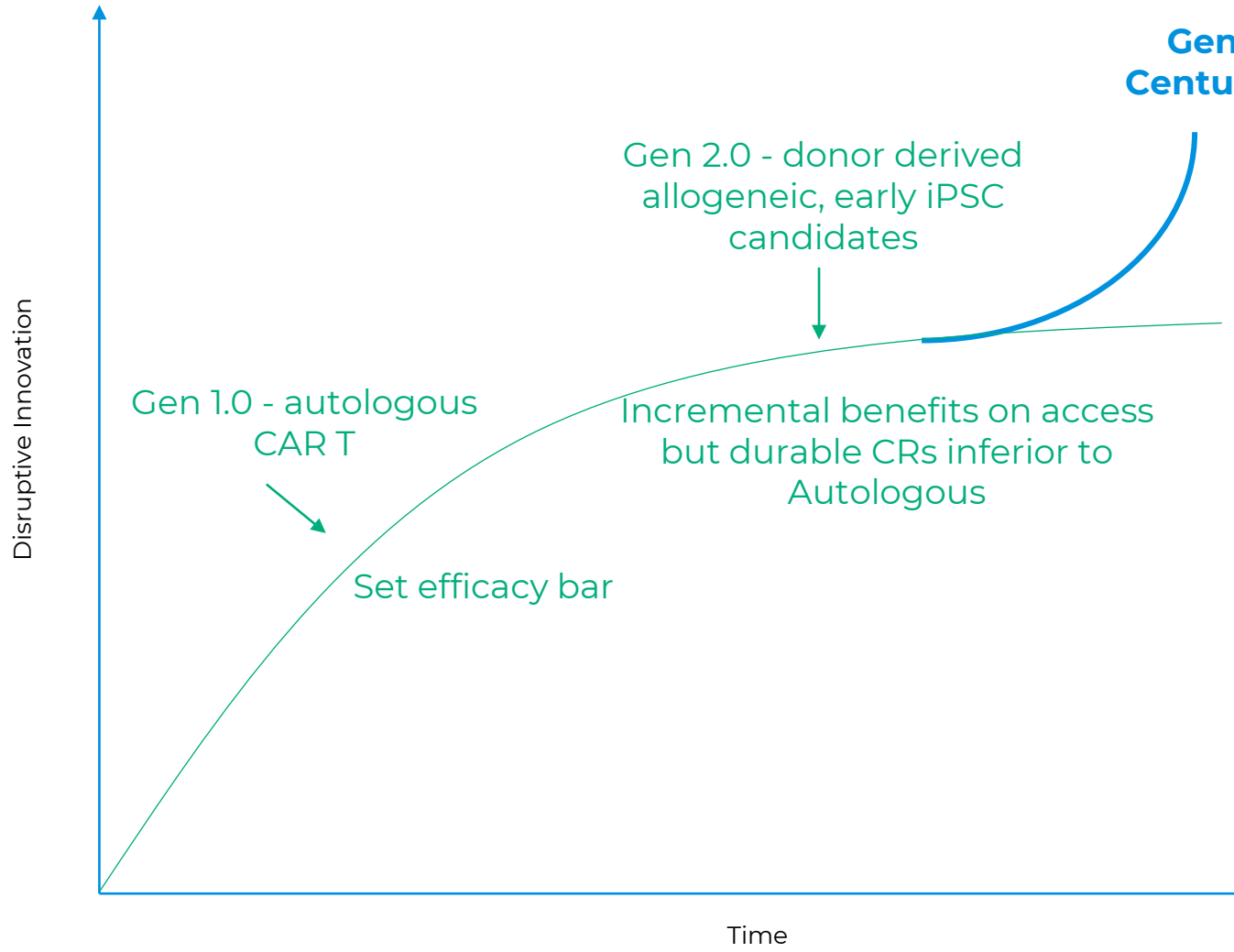
Address heterogeneity via multi-tumor antigen targeting and safety and technical trafficking challenges with locoregional delivery

Nectin-4 + Solid tumors

CNTY-107: Nectin-4 targeted CAR GD iT

Leveraging gamma delta iT platform designed to address several solid tumor indications with high expression of Nectin-4 and unmet need

Leapfrogging the Competition in Lymphoma

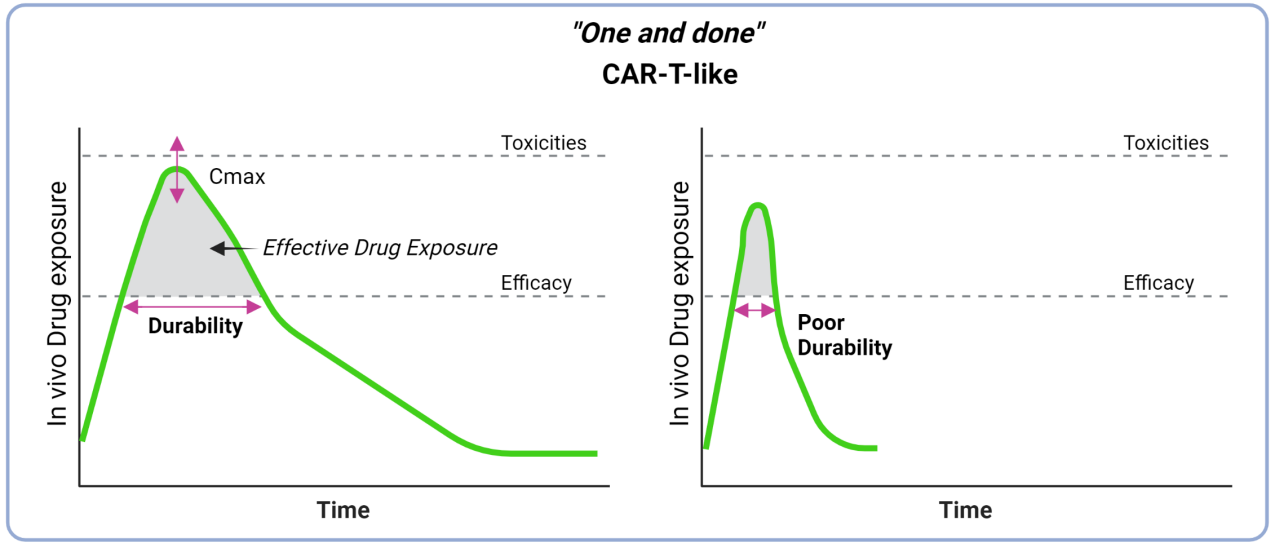


Large opportunity for products that can exceed the Autologous efficacy bar.

Leverage iPSC technology to develop products

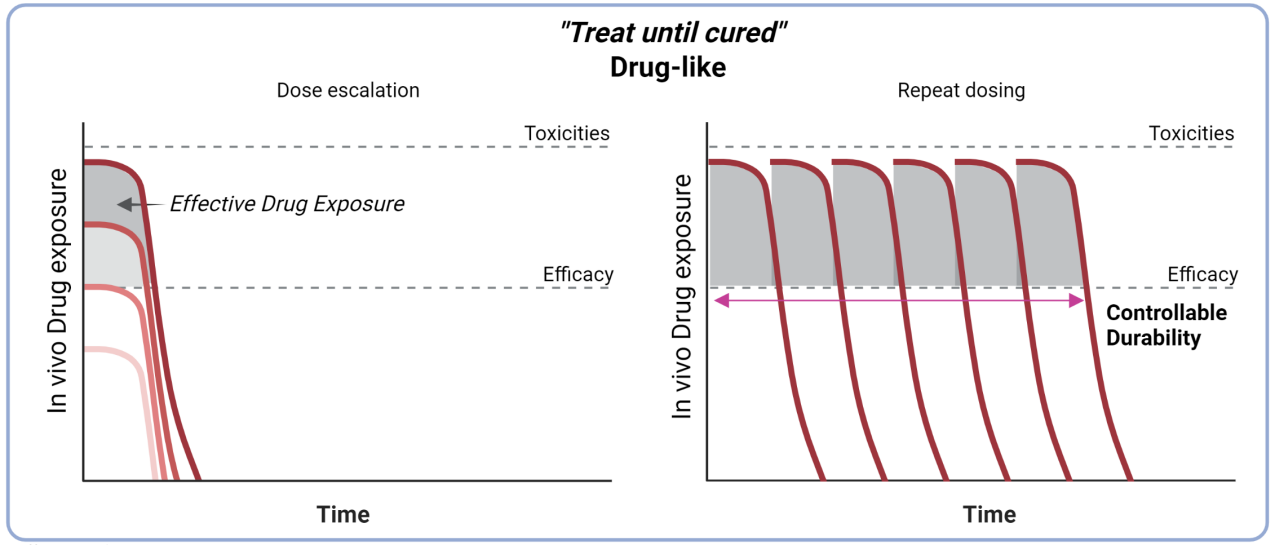
- With multiple enhancements introduced with precision CRISPR gene editing
- That can be manufactured at scale with antibody-like COGs
- That can realize the durability benefit of repeat dosing because they can resist rejection

Transforming the cell therapy treatment paradigm



- AUC main predictor of duration of response
- Variable cell expansion/exposure drives toxicity and suboptimal responses

Single dose of allogeneic NK cells unlikely to match αβ autologous CAR T



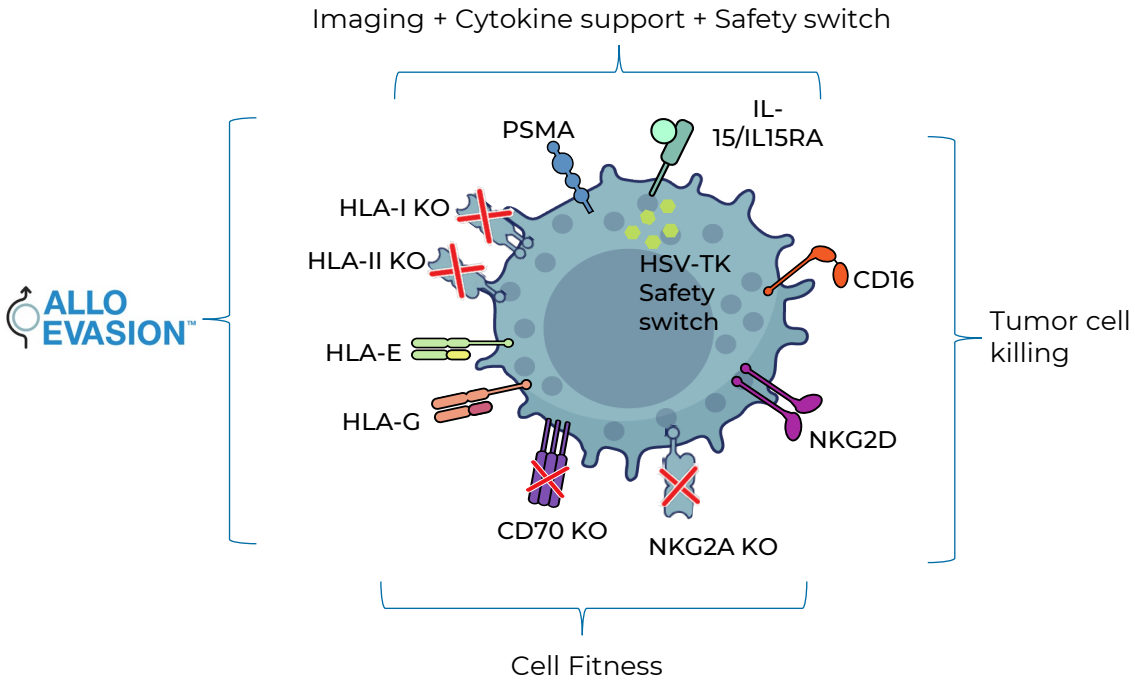
- Finite repeat dosing regimens have the potential to exceed bar set by autologous cell therapy and deliver more durable responses, **if** the cells are engineered to avoid host rejection (Allo-Evasion™)

Illustrative curves

Advances with iNK and iT Cell Platforms Showcased at SITC

iNK 3.0

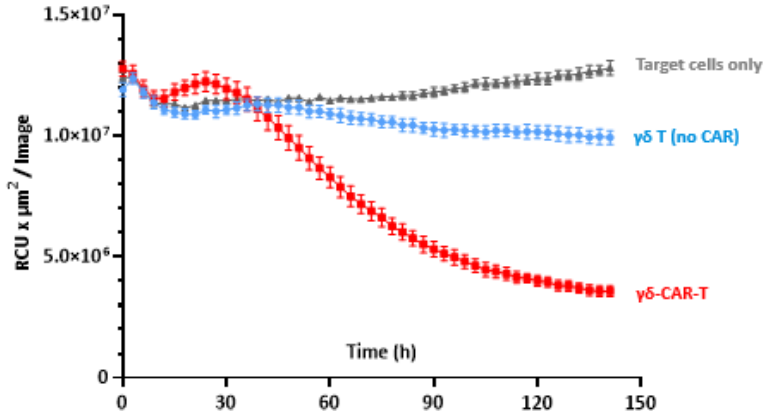
Empowering iPSC-Derived iNK Cells with Multiple Gene Edits to Improve Persistence and Anti-Tumor Efficacy (SITC Abstract 265)



Clonal iPSC line with 11 total genetic modifications show enhanced functionality in iNK 3.0 common progenitor

γδ iT

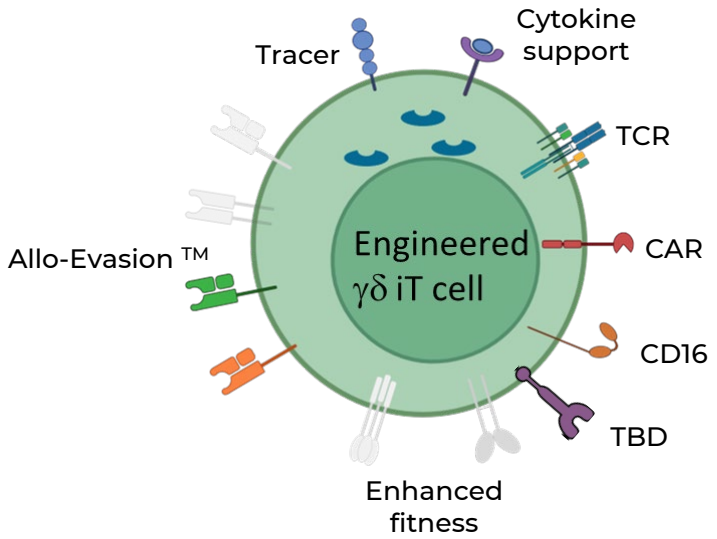
Multiple Targeting of Solid Tumors with iPSC-derived Gamma Delta CAR T Cells in Combination with Therapeutic Antibodies (SITC Abstract 262)



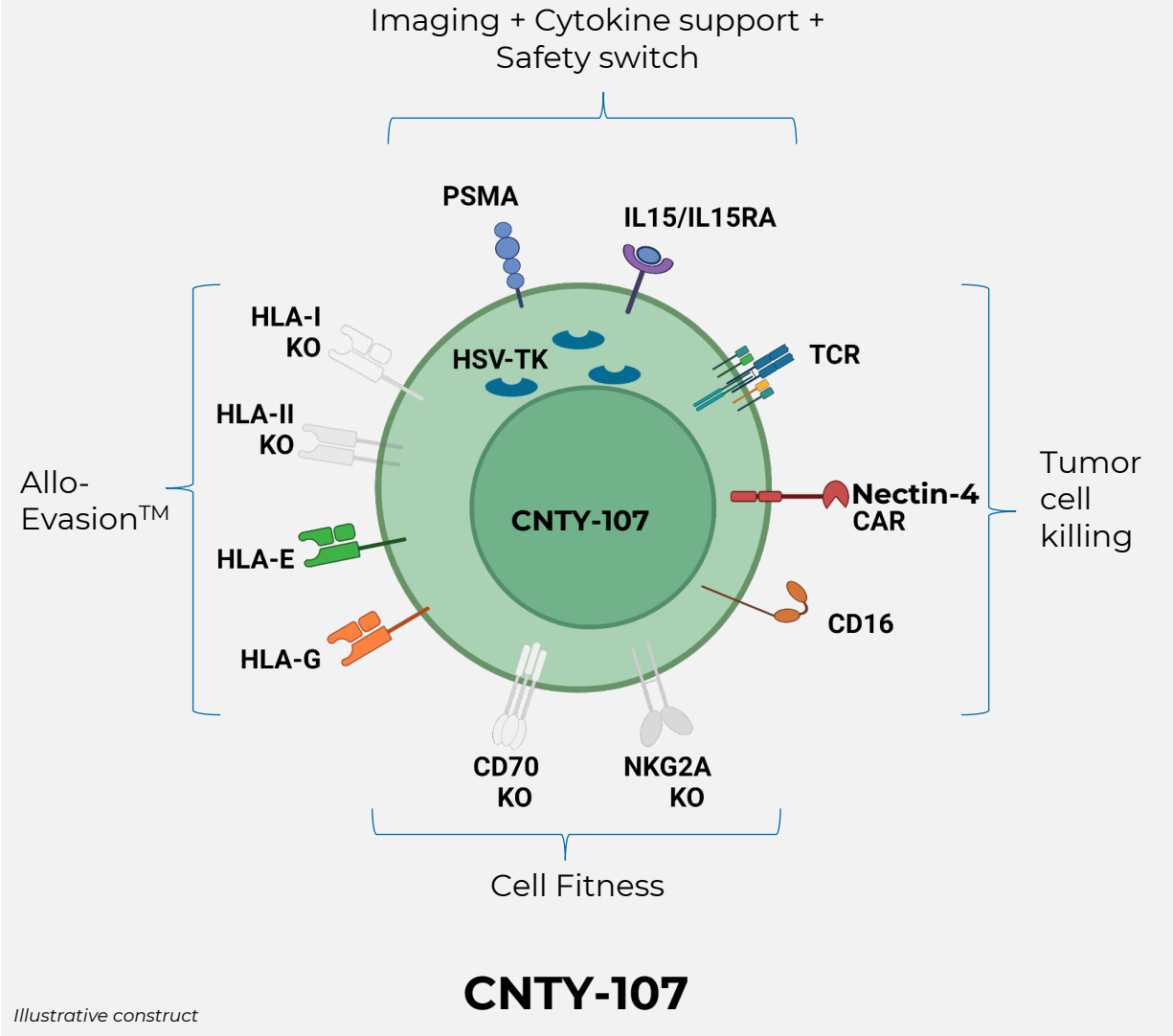
γδ-EGFR-CAR-T cells demonstrate significant CAR-specific killing of ovarian tumor spheroids

Winning in Solid Tumors

Challenges	Century's Solution
Trafficking and infiltration	γδ iT cells - tissue homing
Tumor heterogeneity	• Engage endogenous immunity • Multi tumor targeting pathways
Requirement for chemotherapy conditioning	• Novel conditioning regimens • Genetic engineering
TME / Immunosuppressive environment	Future engineering strategies



CNTY-107: First in Class Nectin-4 Targeted GD iT Cell Therapy



Nectin-4 has been validated by ADC approaches

- Opportunity to address multiple Nectin-4 positive solid tumors
  - Potential indications include bladder, breast, pancreatic, non-small cell lung cancer, esophageal/gastric, head and neck, and/or ovarian cancers

GD iT allogeneic therapies provide potential to improve upon ADC toxicity profile and efficacy

- Intrinsic homing of GD iT cells to tissues and solid malignancies

- Multi-tumor killing modalities to tackle heterogeneity

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	Cleared to proceed 3Q22				
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
CNTY-107	iT	Nectin-4	Solid Tumors	2025				
Discovery Research Programs								
	iNK	TBD	Hematological Tumors	2023				
	iT	TBD	Solid Tumors	TBD				

Anticipated Catalysts Over Next 12 Months

Underpinned by strong balance sheet with platform synergies and operational excellence

CNTY-101

- Phase 1 (ELiPSE-1) trial initiation in B-cell malignancies (by YE22)

CNTY-101 Follow On (CNTY-102)

- Present pre-clinical data at major medical meeting (2H23)

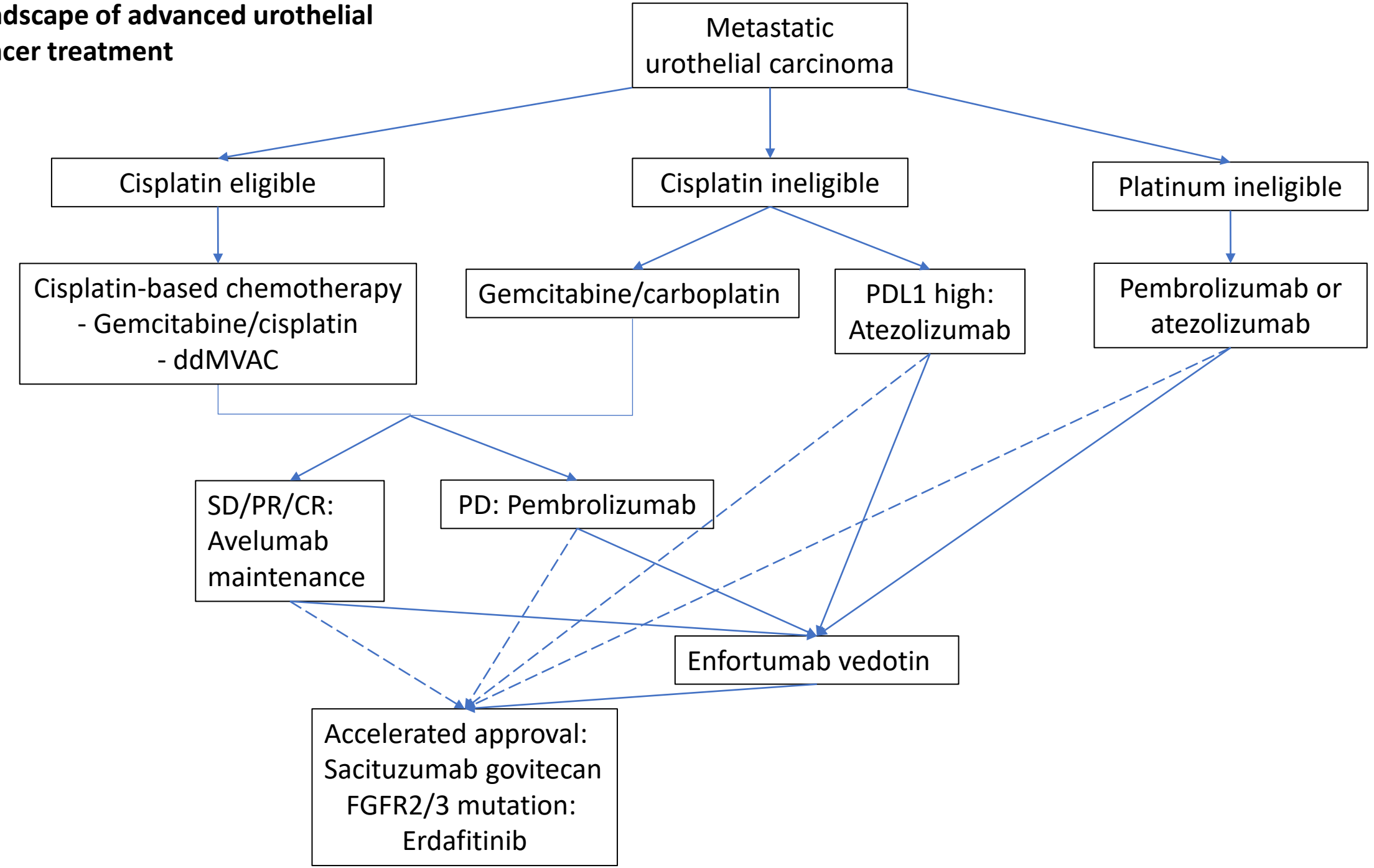
CNTY-103

- Disclose pre-clinical data of development candidate at major medical meeting (2H23)

Nectin-4 directed therapies: Urothelial cancer and beyond

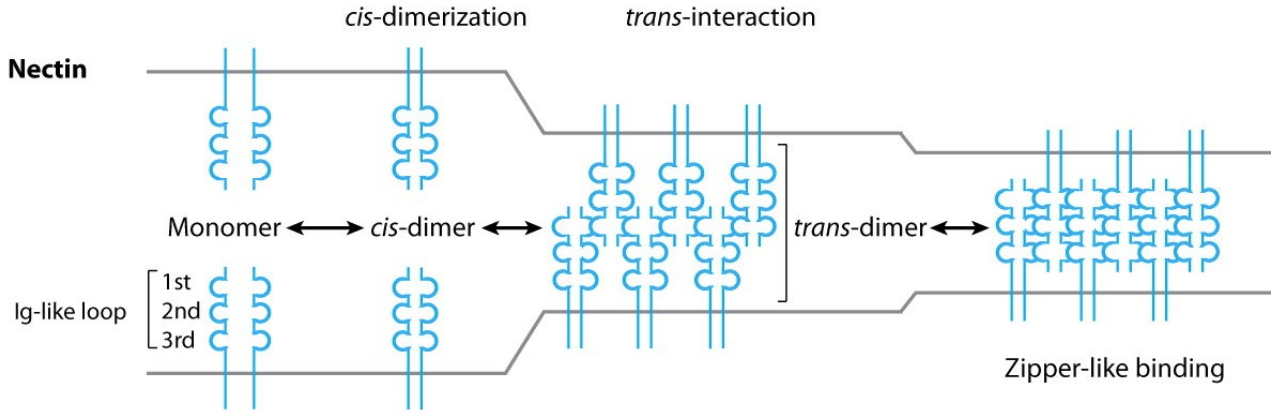
Jonathan Rosenberg, MD
Chief, Genitourinary Oncology Service
Memorial Sloan Kettering Cancer Center
New York, NY

Landscape of advanced urothelial cancer treatment



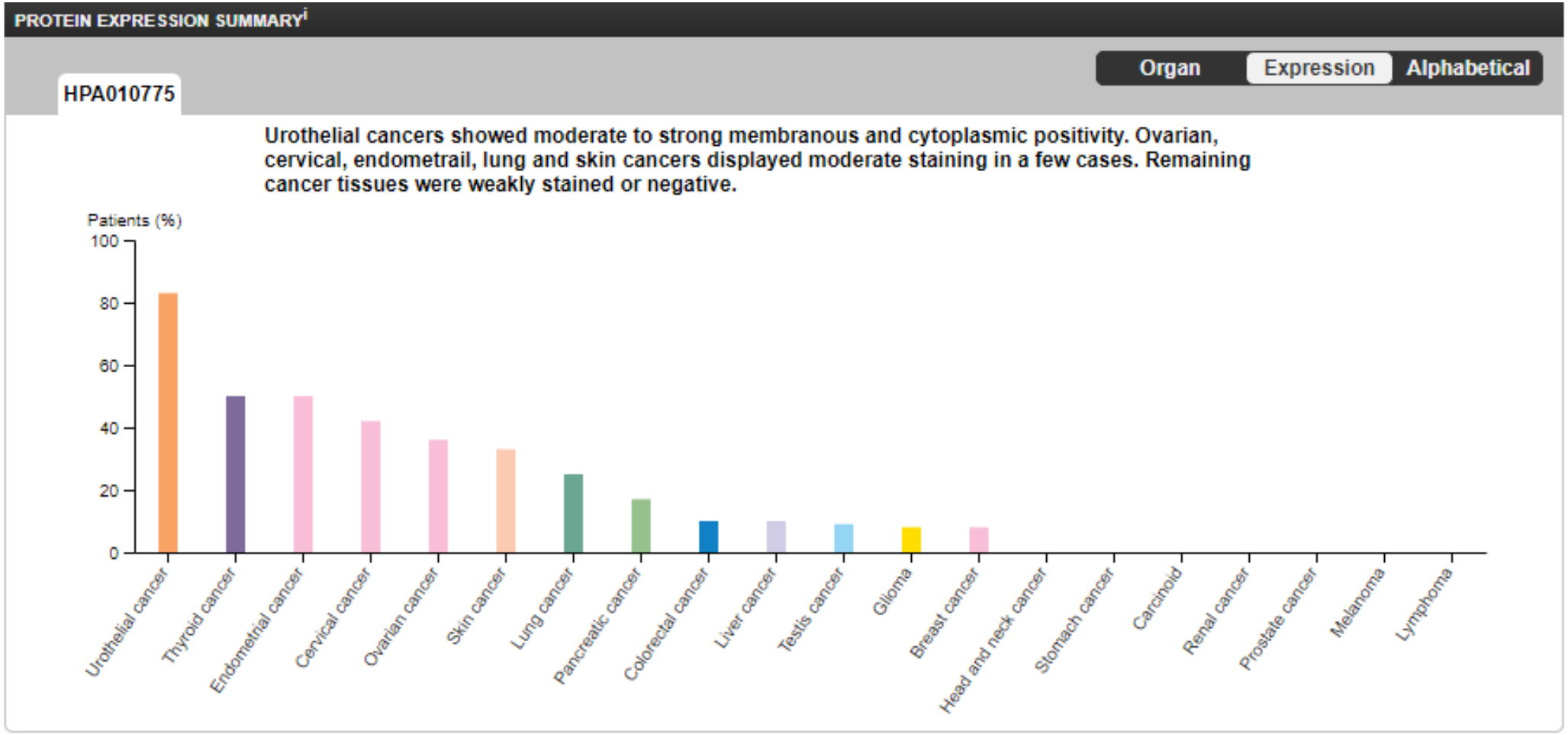
Nectin-4

- Calcium-independent immunoglobulin-like cell adhesion molecule
- Nectins are cell surface protein involved in polarity, proliferation, differentiation, and migration
  - Expressed during development in multiple cell types (epithelial, immune, neuronal)
- Nectin-4 expression is evident in multiple cancers, although restricted in normal tissues
  - Soluble nectin-4 is potential prognostic biomarker in breast and gastric cancer
  - Overexpression in multiple cancers including breast, gastric, urothelial, biliary, and ovarian cancers
  - Normal tissue expression in skin, cornea (low levels), esophagus



Takai, et al. *Annu Rev Cell Dev Biol*. 2008;24:309-42.
Fabre-Lafay, et al. *BMC Cancer*. 2007;7:73
Okumura et al. *Cornea*. 2018;37:633-640
Zhang et al. *Oncol Lett*. 2018;15:8789-8795

Nectin-4 prevalence in cancer



Source: https://www.proteinatlas.org/ENSG00000143217-NECTIN4/pathology

Nectin-4 prevalence in cancer

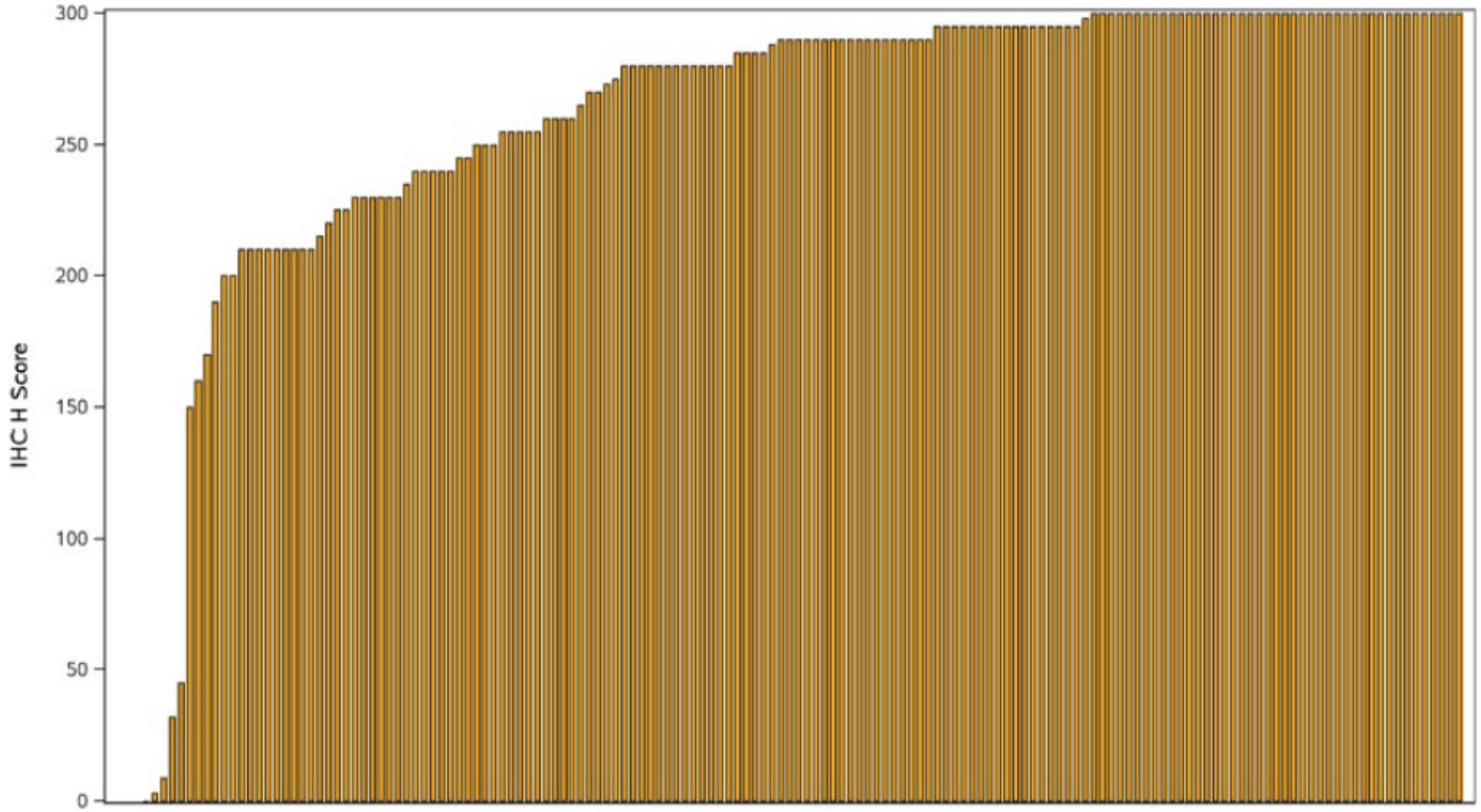
	N	%	Ab used	Ref
Head and Neck Squamous cell ancer	159	13.8% negative 53.5% weak 32.7% medium-high	Abcam clone EPR15613-68	Oncotarget. 2022; 13:1166-1173
Esophageal cancer	92	66% H score ≥70	AF2659	*Cancer Cell Int*. 2019; 19:106
Luminal B Her2 Negative Breast cancer	147	IRS scores: 23.8% negative 18.3% low 40.1% moderate 17.7% high	clone N4.61 (MERCK, DAB150)	*Pathol Res Pract*. 2017; 213:1102-1108
Breast cancer	140	64.3% positive 35.7% negative	AF2659	*Folia Histo Cyto 2011; 49:26–33*
Non-small cell lung cancer	422	58% strong positive 28% weak Positive 14% absent	clone 19–33	*Cancer Res*. 2009. 15; 69: 6694-703

Nectin-4 staining* in urothelial cancer

Required in EV-101 (phase I study of EV in urothelial and other Nectin-4 positive cancers)

Urothelial cancer:
Median H-score, 290; range, 0-300;
4th percentile H-score, 150

EV-201: median H-score 275



EV 101: *J Clin Oncol* 2020 38 1041-1049
EV 201: *J Clin Oncol* 2021 39 6_suppl 394

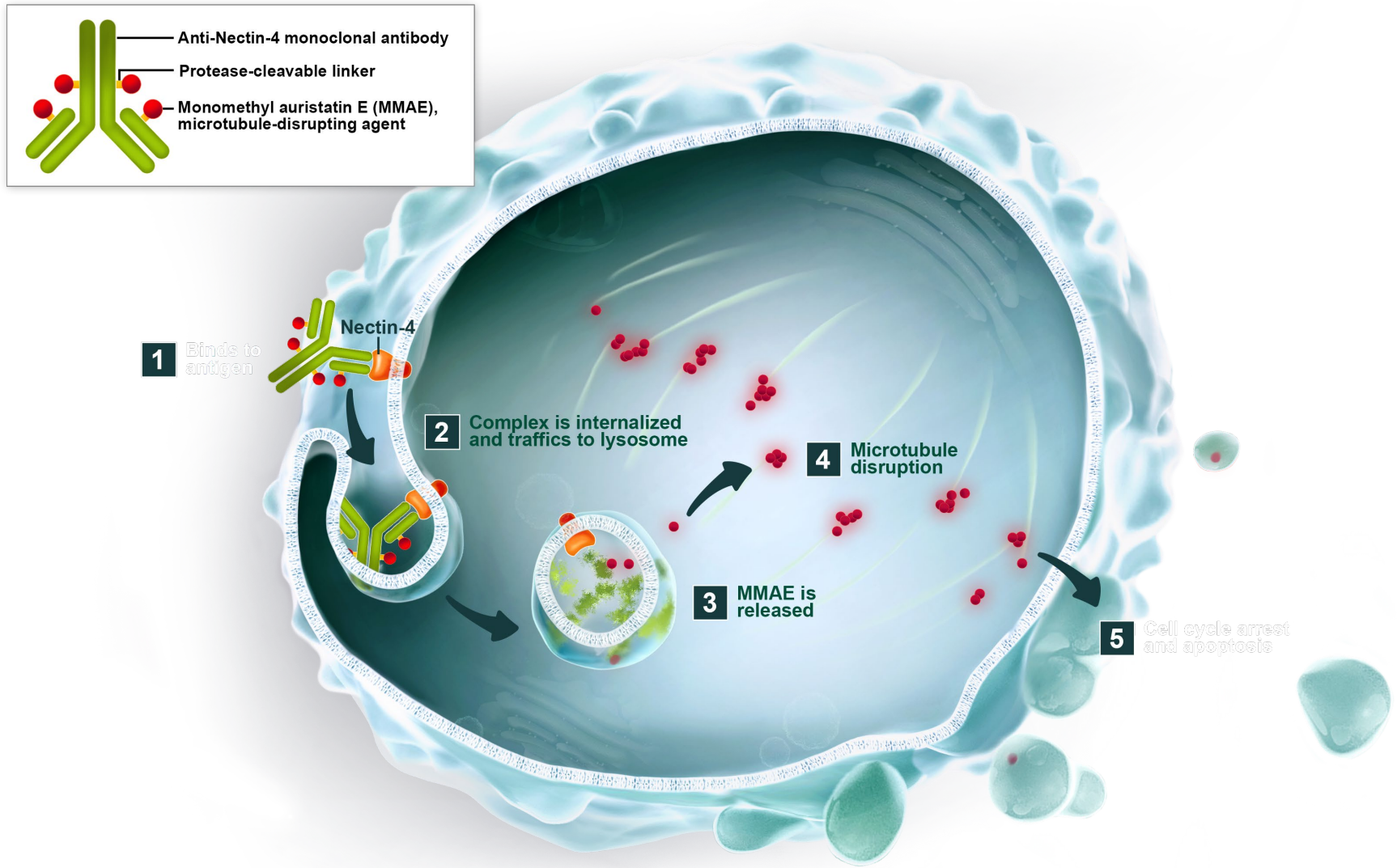
*M22-321b41.1 (developed by Agensys, not commercially available)

Nectin-4: role in cancer

- Nectin-4 knockdown reduces migration, spheroid formation, cell proliferation
- Plays a role in epithelial-mesenchymal transition
- Upon association with Afadin, Nectin-4 induces PI3K/AKT activation, and cellular proliferation via PI3K/AKT pathway
- Nectin-4 interacts with ERBB2 and trastuzumab resistant splice variants, and leads to activation of PI3K/AKT signaling
- Implicated in stemness, angiogenesis, and metastasis

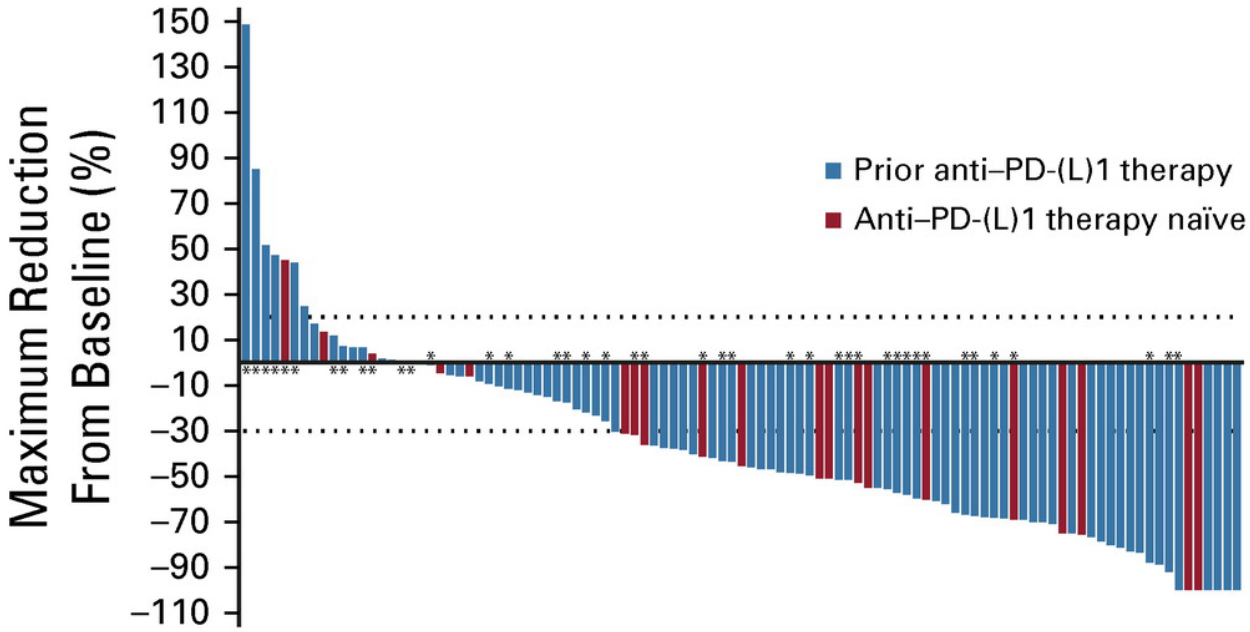
Boylan, et al. Oncotarget. 2017; 8:9717-9738
Siddarth et al. Int J Biochem Cell biol. 2017; 89:985-94
Zhang, et al. Hum Pathol. 2018;72:107-116
Kedashiro et al. Sci Rep. 2019;9:18997

Enfortumab Vedotin: Nectin-4 Targeted Therapy

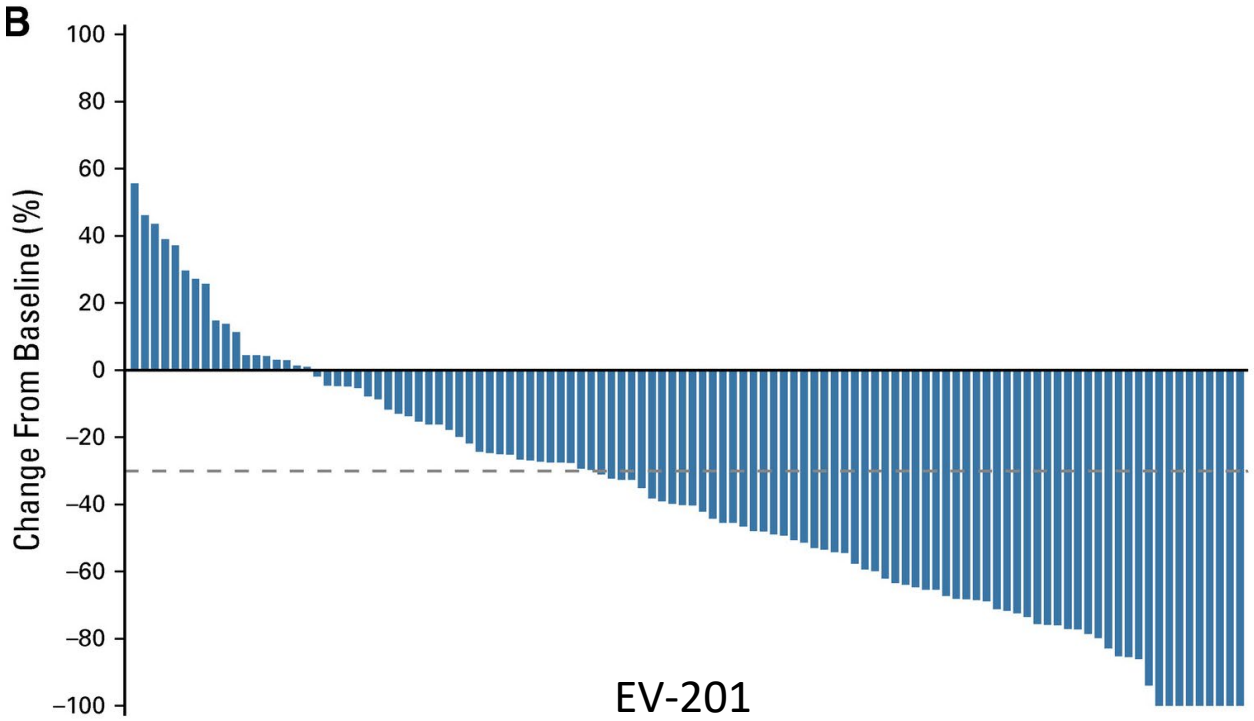


Enfortumab vedotin (ASG-22ME) is an investigational agent, and its safety and efficacy have not been established.
Enfortumab vedotin is being developed in collaboration with Astella... ...19 Seattle Genetics, Inc. All rights r...ed.

Enfortumab vedotin anti-tumor activity

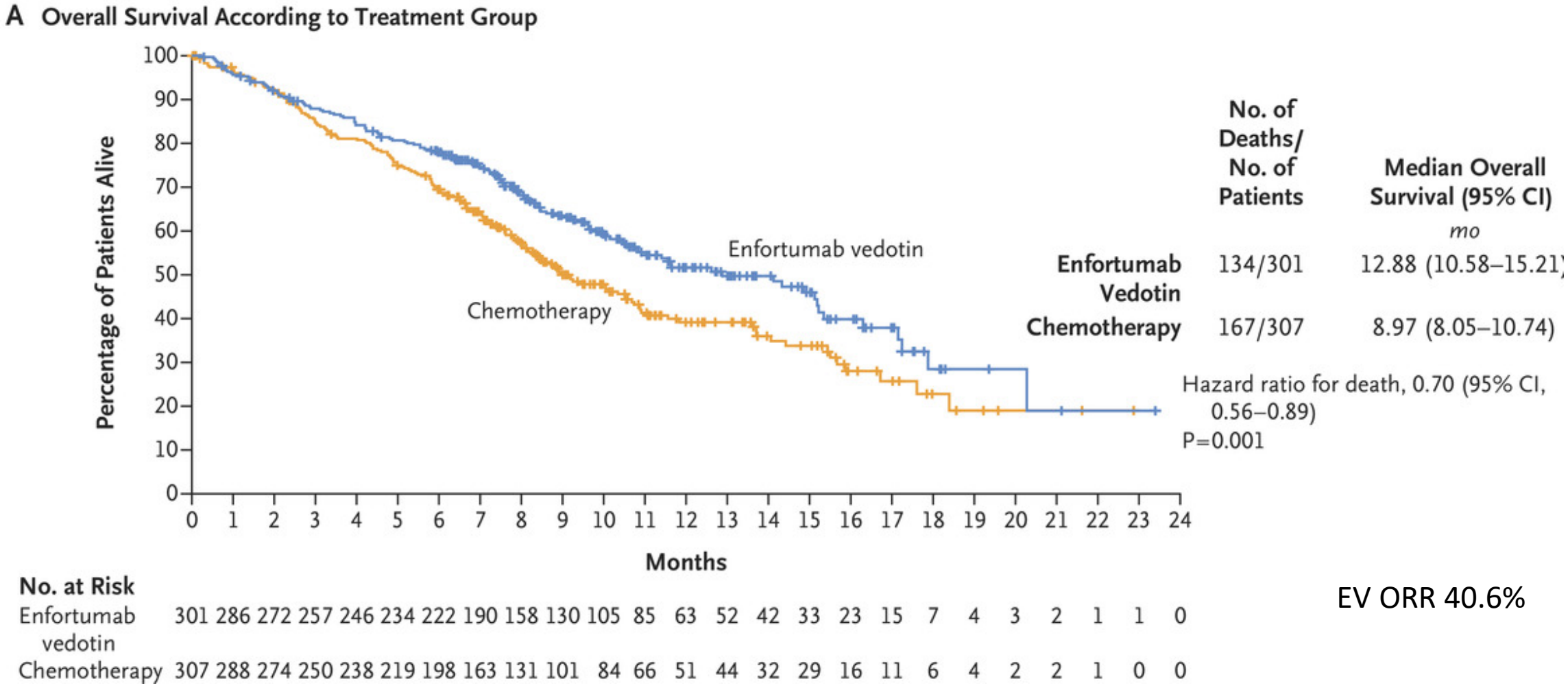


EV-101
Phase I
ORR 43%



EV-201
Phase 2
ORR 44%

EV-301: EV improves survival compared to standard chemotherapy



EV ORR 40.6%

PFS 5.55 vs. 3.71 months; hazard ratio for progression or death, 0.62; 95% CI, 0.51 to 0.75; P<0.001)

Powles, Rosenberg, et al. *NEJM* 2021

Common enfortumab vedotin toxicities include fatigue, rash, neuropathy; hyperglycemia occurs and may be severe

Table 2. Treatment-Related Adverse Events (Safety Population).*

Adverse Event	Enfortumab Vedotin Group (N=296)		Chemotherapy Group (N=291)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Any adverse event	278 (93.9)	152 (51.4)	267 (91.8)	145 (49.8)
Alopecia	134 (45.3)	0	106 (36.4)	0
Peripheral sensory neuropathy†	100 (33.8)	9 (3.0)	62 (21.3)	6 (2.1)
Pruritus	95 (32.1)	4 (1.4)	13 (4.5)	0
Fatigue	92 (31.1)	19 (6.4)	66 (22.7)	13 (4.5)
Decreased appetite	91 (30.7)	9 (3.0)	68 (23.4)	5 (1.7)
Diarrhea	72 (24.3)	10 (3.4)	48 (16.5)	5 (1.7)
Dysgeusia	72 (24.3)	0	21 (7.2)	0
Nausea	67 (22.6)	3 (1.0)	63 (21.6)	4 (1.4)
Maculopapular rash	48 (16.2)	22 (7.4)	5 (1.7)	0
Anemia	34 (11.5)	8 (2.7)	59 (20.3)	22 (7.6)
Decreased neutrophil count	30 (10.1)	18 (6.1)	49 (16.8)	39 (13.4)
Neutropenia	20 (6.8)	14 (4.7)	24 (8.2)	18 (6.2)
Decreased white-cell count	16 (5.4)	4 (1.4)	31 (10.7)	20 (6.9)
Febrile neutropenia	2 (0.7)	2 (0.7)	16 (5.5)	16 (5.5)

Powles and Rosenberg, et al. *NEJM* 2021

MMAE Payload-related side effects

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Powles and Rosenberg, et al. *NEJM* 2021

Nectin-4 on-target side effects

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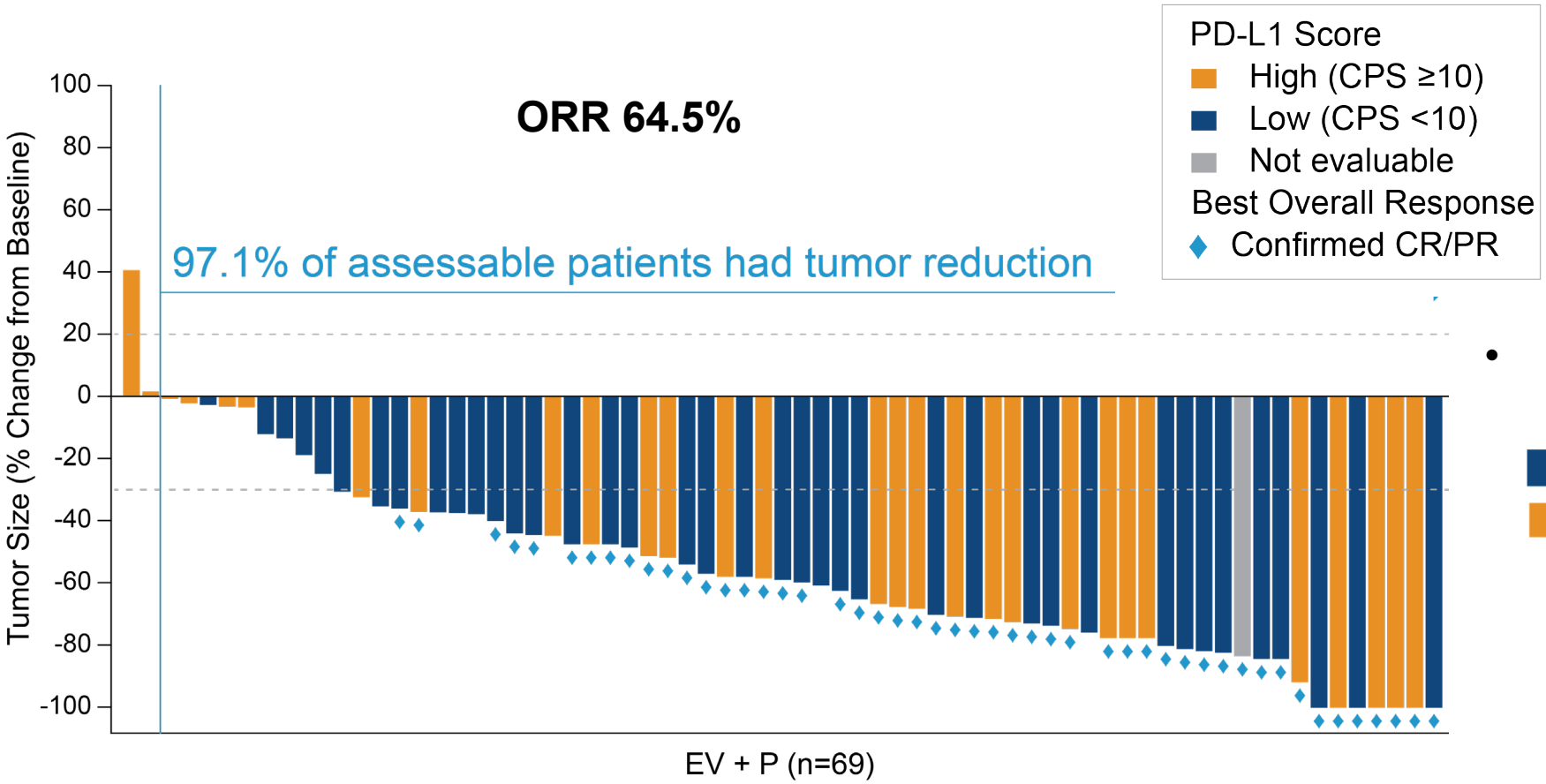
Febrile neutropenia	2 (0.7)	2 (0.7)	16 (5.5)	16 (5.5)

Overlapping?

Powles and Rosenberg, et al. *NEJM* 2021

EV-103 Cohort K: Enfortumab vedotin + pembrolizumab leads to deep and durable responses in newly diagnosed cisplatin-ineligible patients with advanced urothelial cancer



BICR: Blinded Independent Central Review; CPS: Combined Positive Score; CR: Complete Response; PD-L1: Programmed Death-Ligand 1 PR: Partial Response

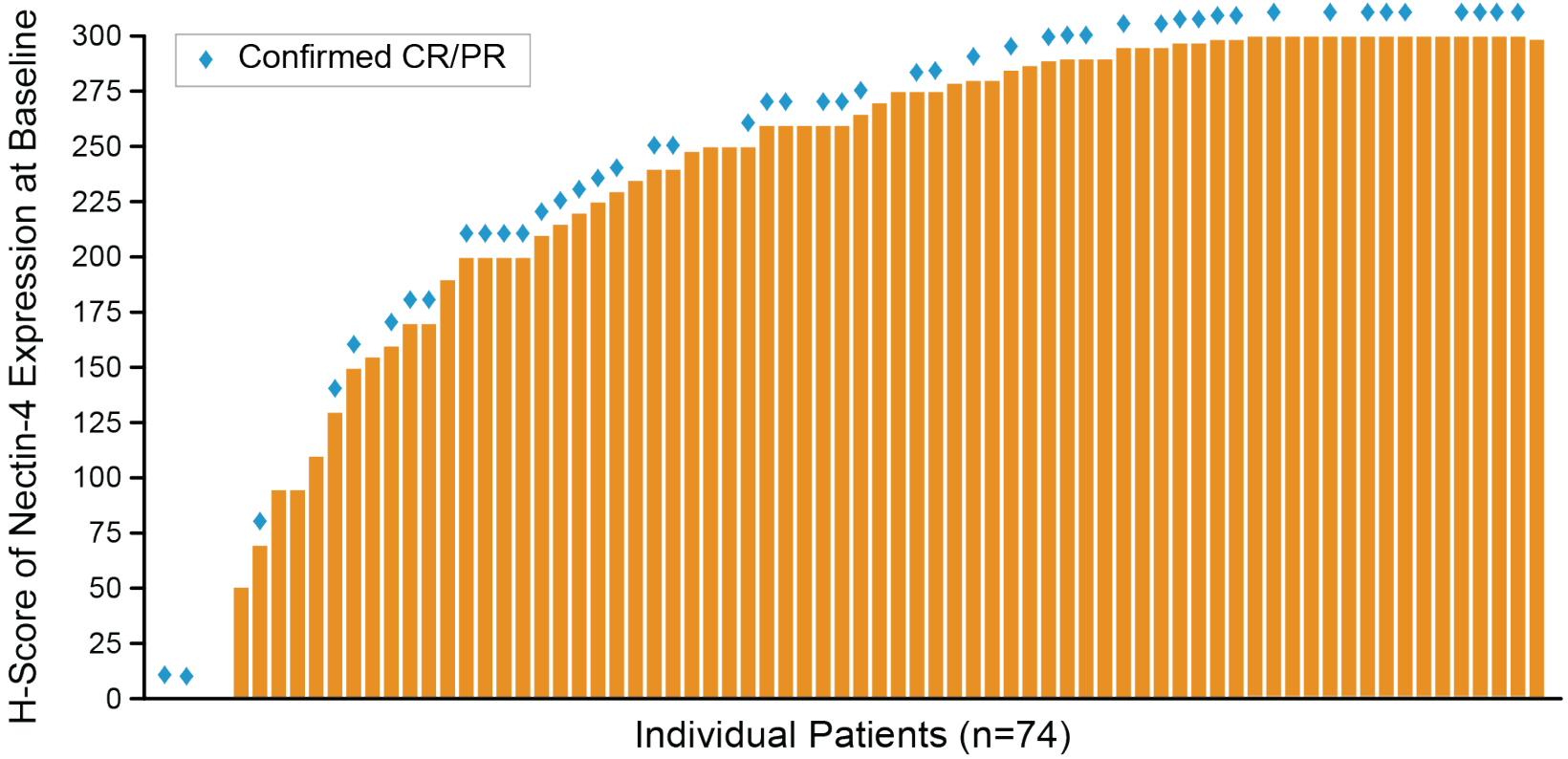
- Activity seen regardless of PD-L1 status
  - 27/44 (61.4%) cORR in CPS<10
  - 21/31 (67.7%) cORR in CPS≥10

EV-103 Cohort A:
- ORR 73.3%
- PFS 12.3 mo
- DOR 25.6 mo
- OS 26.1 mo

Hoimes et al. JCO 2022

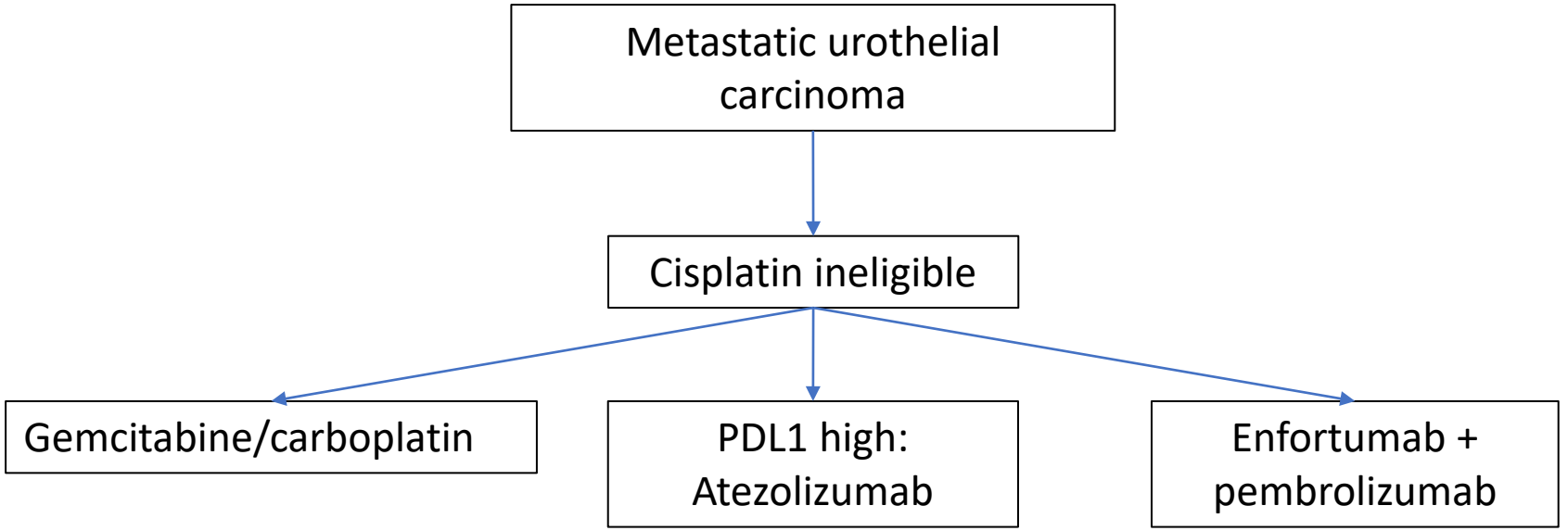
EV+P: Nectin-4 Expression and Best Overall Response

Activity seen regardless of Nectin-4 expression level



- Nectin-4 was detected in tumor tissue from 94.6% of patients who had adequate tissue for testing

Enfortumab moves to first line:
Anticipated accelerated approval with EV-103 Cohort K



Full approval pending results of EV-302 comparing gemcitabine and platinum to enfortumab/pembrolizumab. NCT04223856

Potential mechanisms of resistance to Enfortumab vedotin

- Luminal urothelial cancers may have higher Nectin-4 levels

  Clin Cancer Res. 2021 Sep 15;27(18):5123-5130.

- MDR-1/P-glycoprotein overexpression likely leads to MMAE export from cancer cell

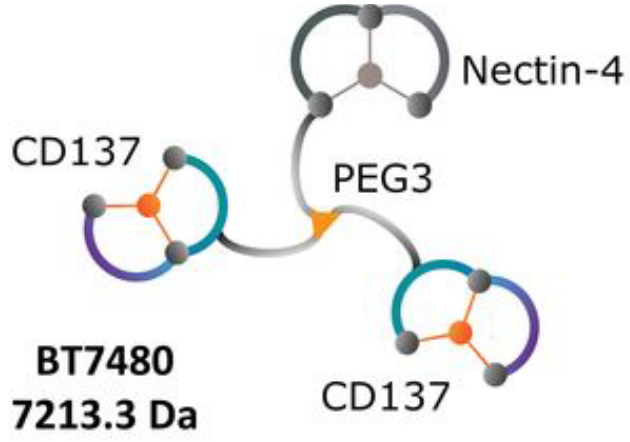
  Mol Cancer Ther. (2022) 21 (7): 1227–1235.

- Downregulation of Nectin-4 expression on cell surface
  - *Eur Urol Oncol*. 2022 Feb 22;S2588-9311 (Online ahead of print).
  - *Clin Cancer Res*. 2021 Sep 15;27(18):5123-5130.

- Clinical data is limited- 3 patients with progression on EV retain Nectin-4 expression in post-treatment biopsies
  - *Urol Oncol*. 2021 39(10): 619-22.

Other Nectin-4 targeted thearpies: bicyclic compounds in early phase trials

- Constrained bicyclic peptides or “bicycles”
- Linear peptide cyclized around a trivalent scaffold
- Can be used to deliver cytotoxics, or bind to other proteins/immune molecules
- Smaller than ADC’s, more able to penetrate tumors



Upadhyaya et al. J Immunother Cancer. 2021;9:e001762
Hurov et al. J Immunother Cancer. 2021;9:e002883
Rigby et al. Mol Cancer Ther. 2022;Epub ahead of print

Future landscape for Nectin-4 directed therapy:

Nectin-4 directed therapy moves earlier in the urothelial cancer disease course

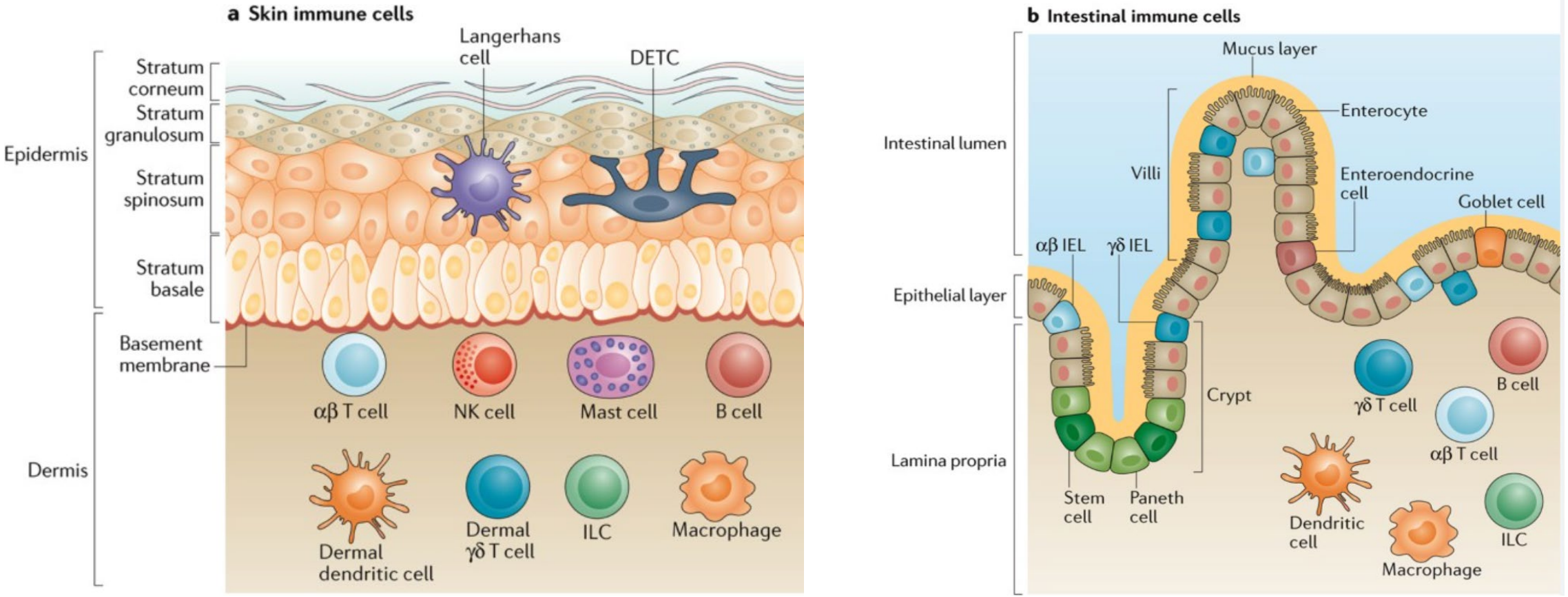
- EV-103 cohort K and EV-302 seek to move EV to first-line therapy
- KN-B15, KN-905 (EV/pembrolizumab) and VOLGA (EV/durva/treme) testing EV in muscle invasive localized disease
- Nectin-4 expression may be preserved in EV refractory tumors
- Subsequent opportunities include late-line disease states
  - Accelerated approval still possible in areas of unmet need (multiply refractory patients)
- EV-202 (NCT04225117)is testing enfortumab in multiple diseases:
  - Breast cancer, lung cancer, gastric/GE junction, esophageal cohorts

CENTURY THERAPEUTICS

Rationale for iPSC-derived γδ CAR-T cells

Hy Levitsky, MD I President, R&D

γδ T cells in Homeostasis and Host Defense of Epithelial Barrier Tissues

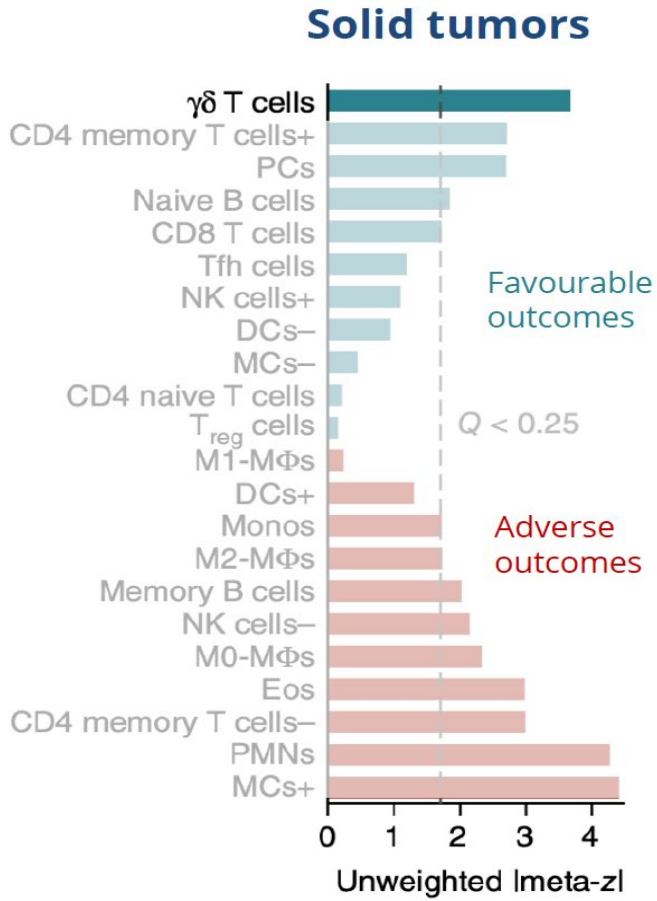


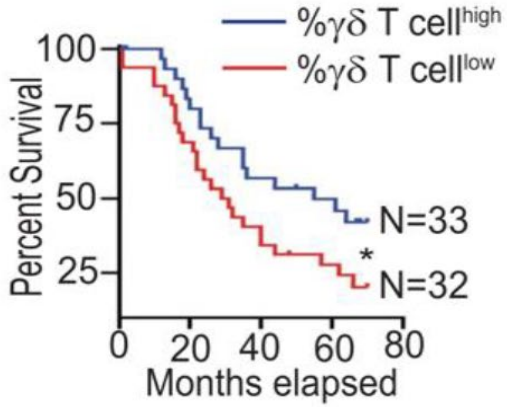
γδ T cells make up between 1-20% of peripheral blood T cells, but comprise the majority of T cells that reside in tissues

Nature Reviews Immunology **volume 17**, pages 733–745 (2017)

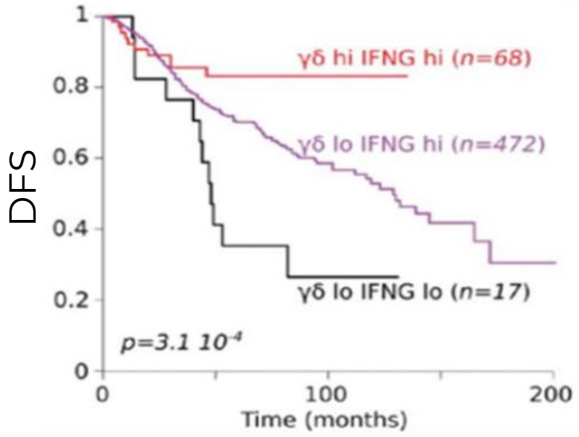
Abundance of γδ T cell in TIL Associated with Favorable Prognosis

18,000 human tumor samples across 39 malignancies





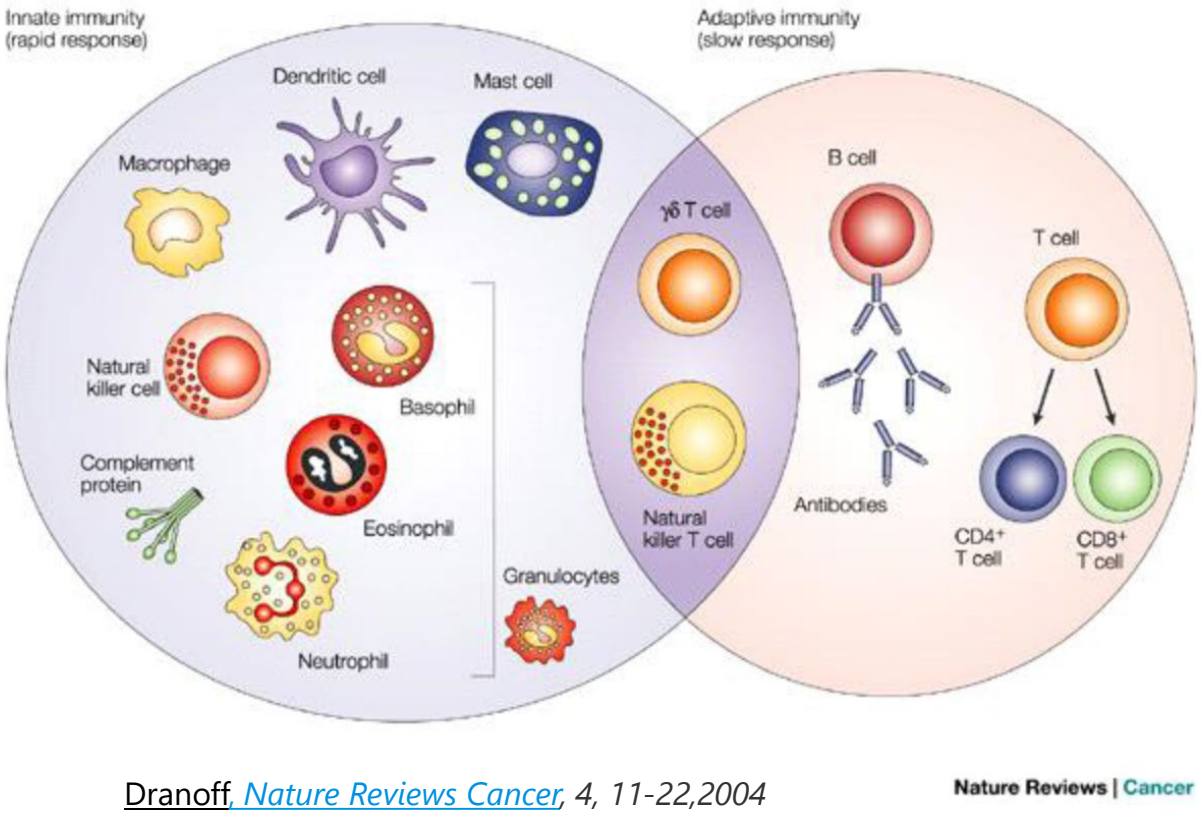
Ovarian Cancer



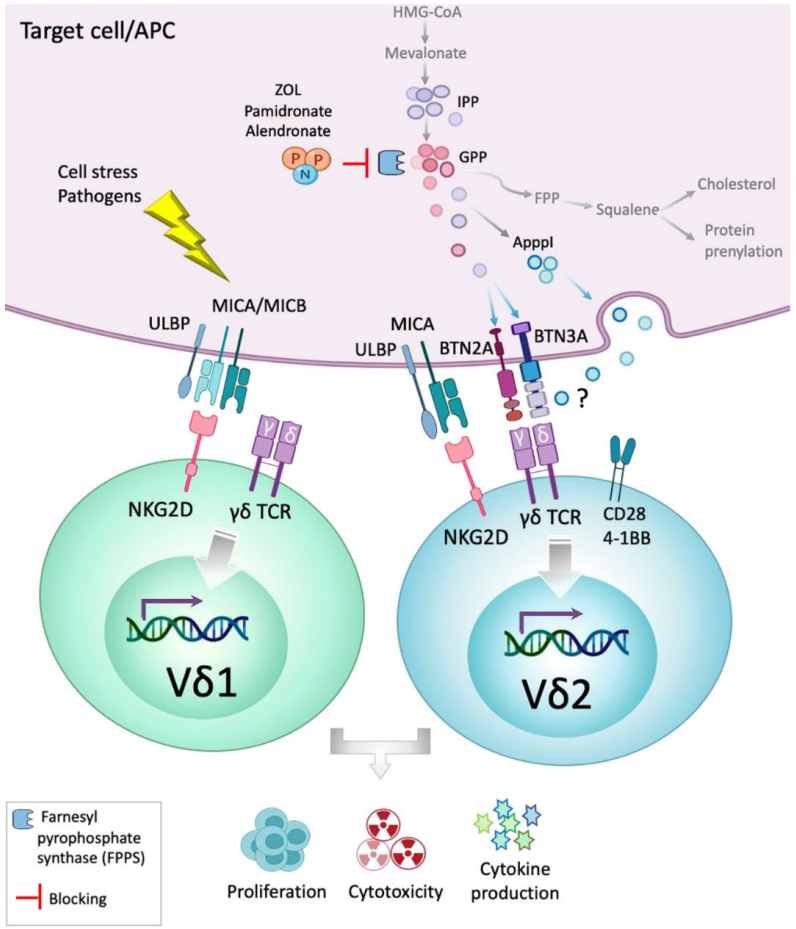
Colorectal Cancer

Gentles et al Nature Med. 2015; Payne et al Science 2020; Meraviglia et al Oncoimmunology 2017

γδ T cells: At the Interface of Innate and Adaptive Immunity



Dranoff, *Nature Reviews Cancer*, *4*, 11-22,2004



Yazdanifar et al *Cells* **2020**, *9*(5), 1305

γδ TCRs Do Not Recognize Classical HLA And Are Not Alloreactive

Clinical Evidence

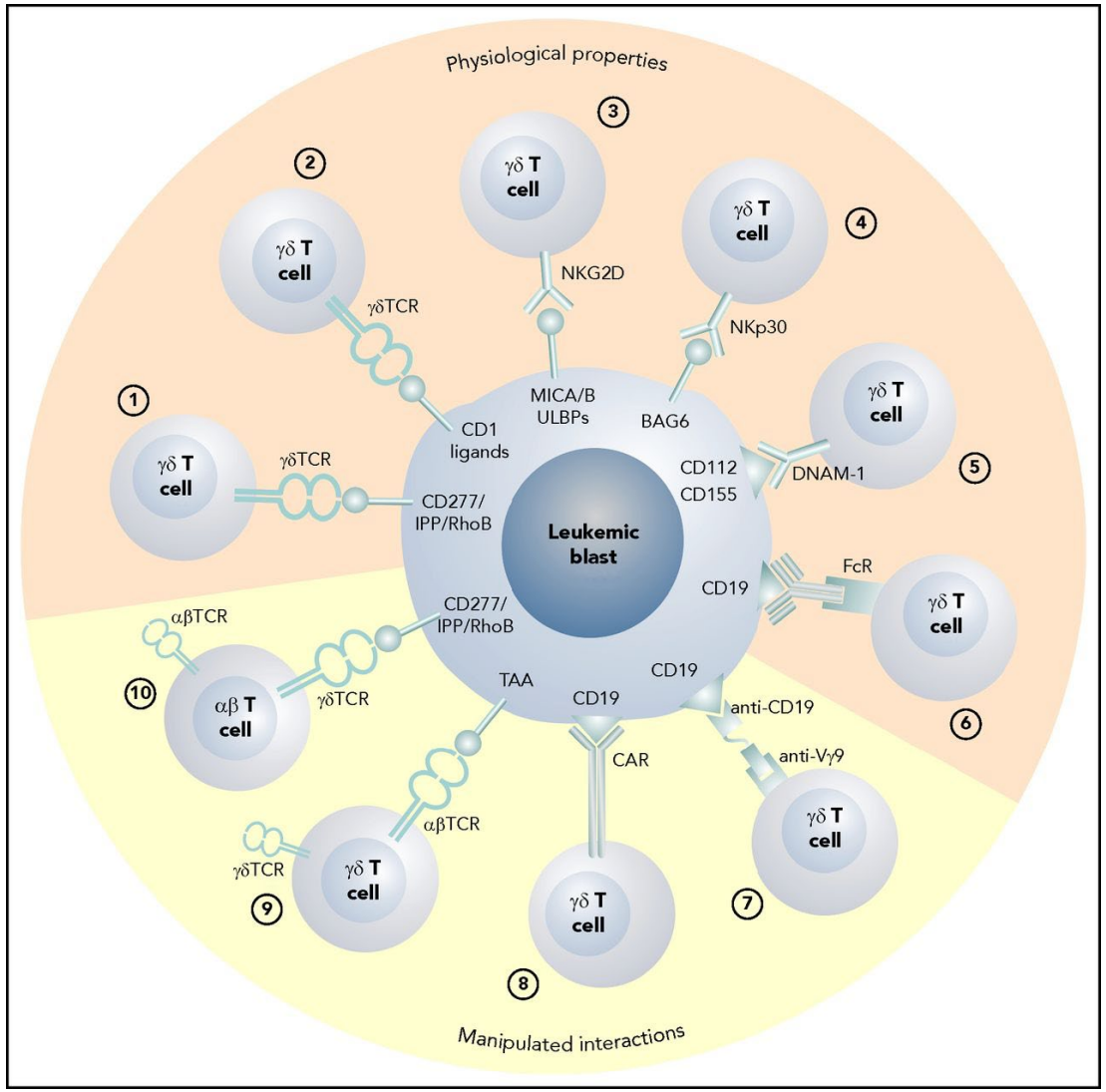
- Partial HLA-mismatched allo-HCT with αβ T cell depleted grafts showed improved DFS as a function of the number of γδ T cells (median 11 x 10^6/kg) infused *with no increase in GVHD*[1-4]
- γδ T cell enriched donor lymphocyte infusion post allo-HST (up to 83 x 10^6/kg), *no GVHD*[5]
- Recent or ongoing studies of adoptive transfer of allogeneic ex vivo expanded γδ T cells (with or without genetic engineering)[6,7,8]

[1]Lamb et al. *Cytotherapy*. 1999;1(1):7-19, [2]Godder et al. *Bone Marrow Transplant*. 2007;39(12):751-757, [3]Otto et al. *J Immunother*. 2005;28(1):73-78, [4]Lang et al. *Bone Marrow Transplant*. 2015;50(Suppl 2):S6-S10, [5]Radestad et al, *J Immunol Res*. 2014:578741

[6]Lin et al., *Signal Transduction Targeted Ther* (2020) 5(1):215, [7]Xu et al, *Cell Mol Immunol* (2021) 18(2):427–39

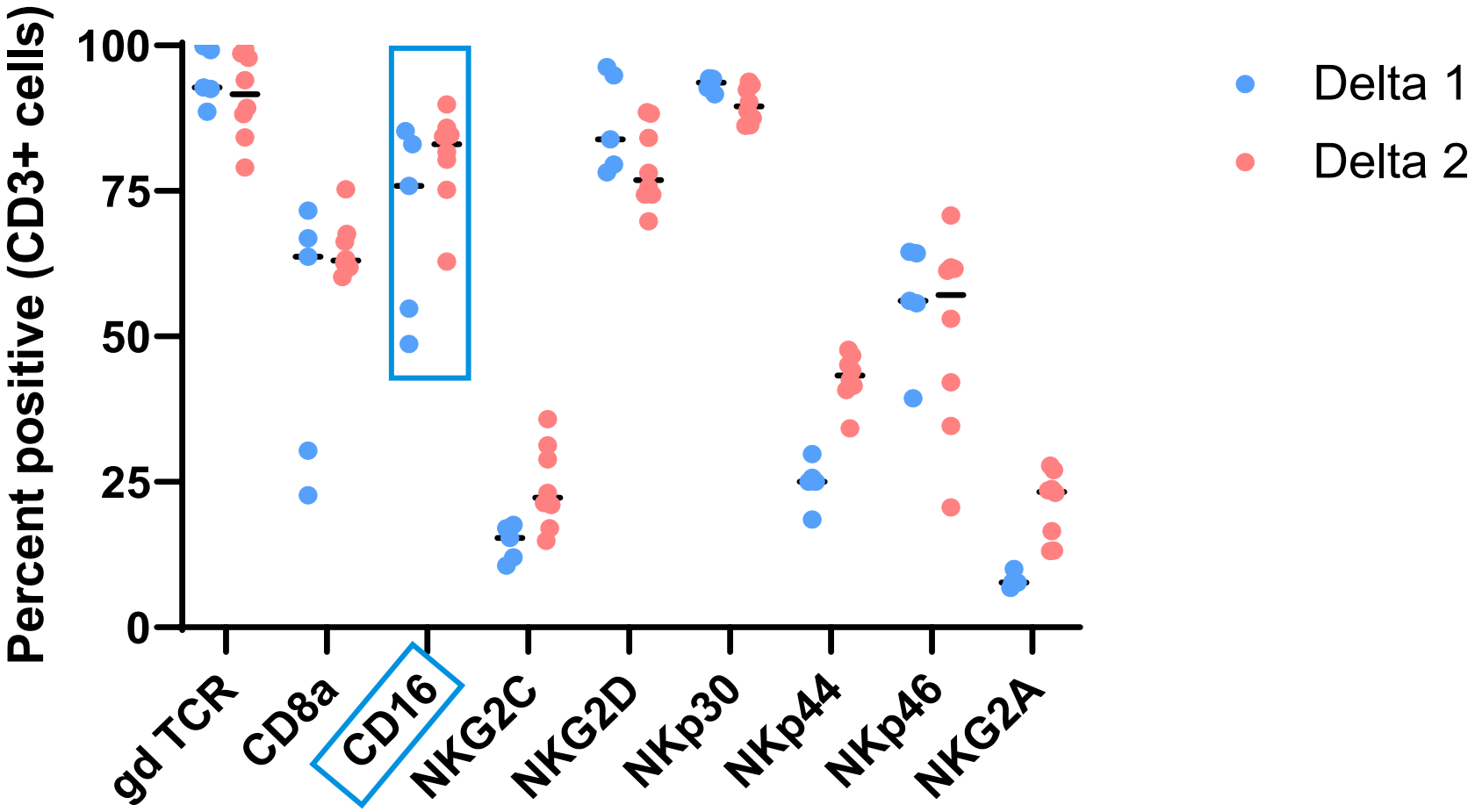
[8] Neelapu, et al. J Clin Oncol 40, 2022 (suppl 16; abstr 7509), Nabors, et al. J Clin Oncol 40, 2022 (suppl 16; abstr 2044), Xu, et al. *Cell Mol Immunol* 2021 Feb;18(2):427-439

Multiple Potential Mechanisms for Tumor Recognition Both Intrinsic and Synthetic



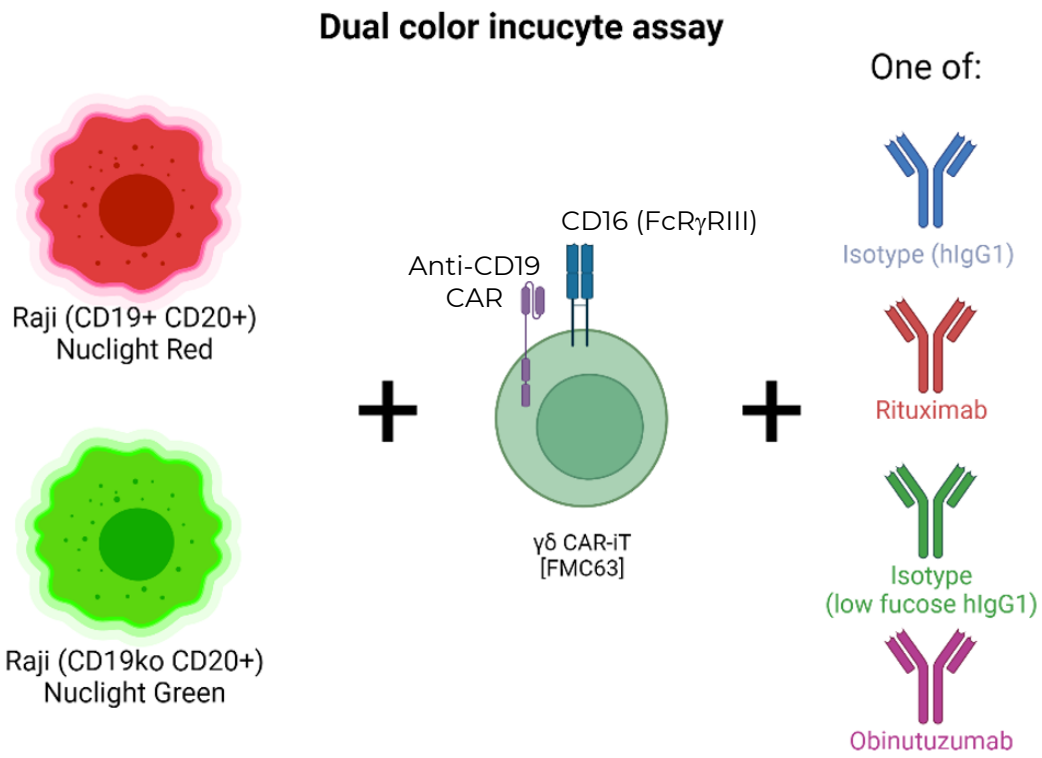
Blood (2018) 131 (10): 1063–1072.

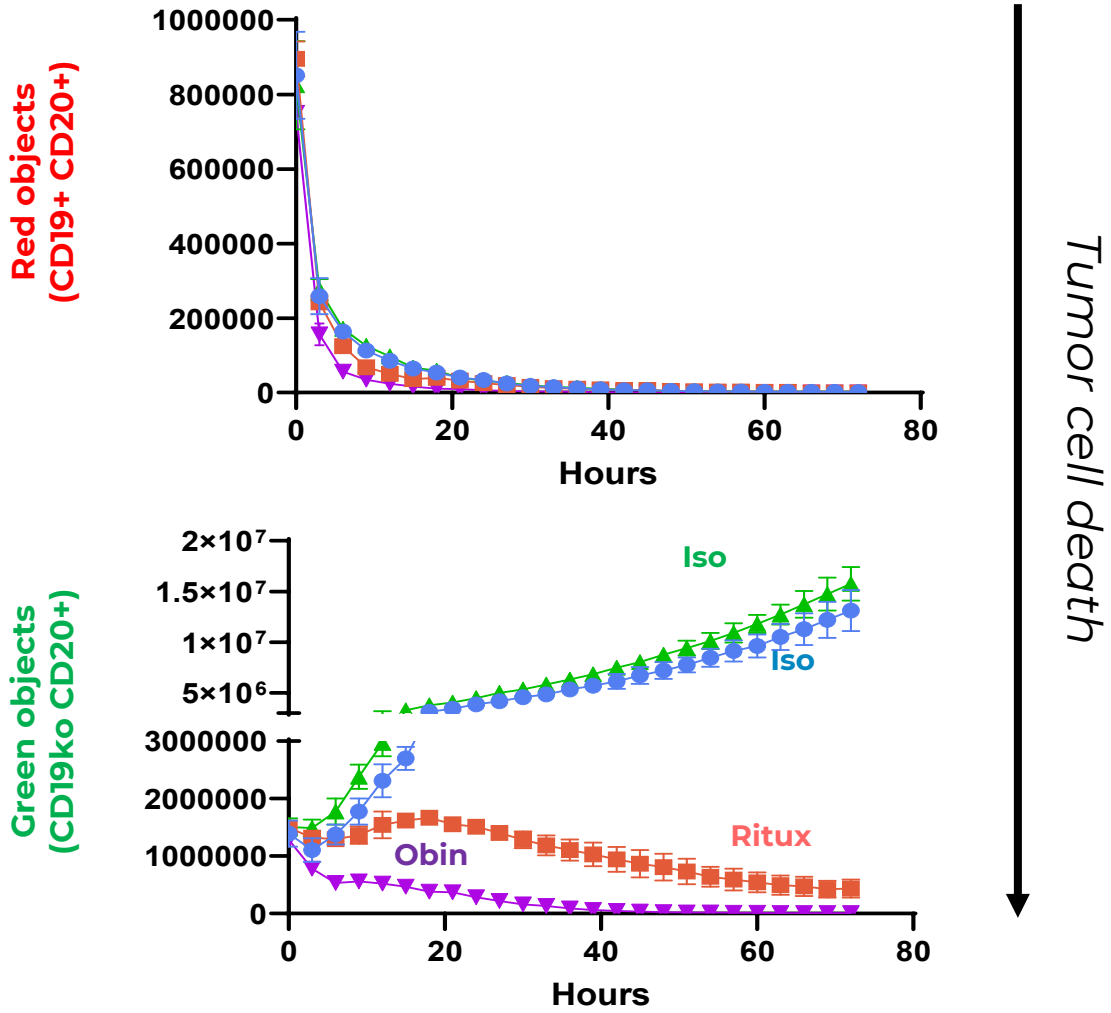
Diverse Innate Mechanisms for Tumor Targeting



N=13 clinical grade TiPSC lines at T cell stage (post differentiation); All lines are Vγ9

γδ CAR-iT cells mediate ADCC





Key Takeaways

The biological properties of γδ T cells make them an ideal platform for genetically modified cell therapy of cancers

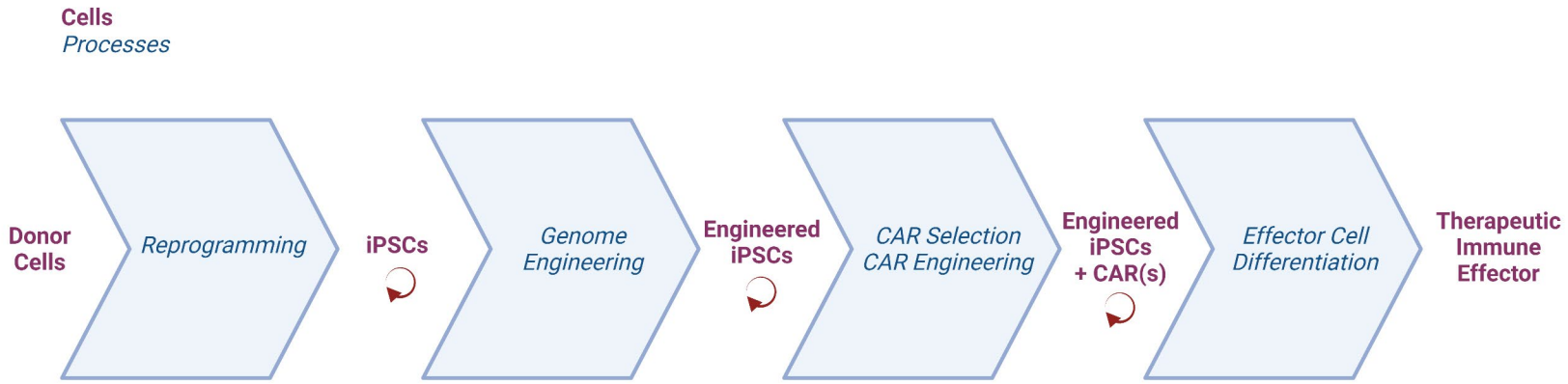
- Innate receptors provide multiple orthogonal mechanisms for tumor recognition
- Functional Fc receptors enable combination therapies with monoclonal antibodies
- Tissue tropism and long-lived persistence favor prolonged tumor surveillance
- Expansion capacity in response to antigen and cytokines mirror αβ T cells (and is > than NK cells)
- Allogeneic sources can be utilized with little risk of GVHD
- Differentiation from iPSCs yields highly potent immune effectors

CENTURY THERAPEUTICS

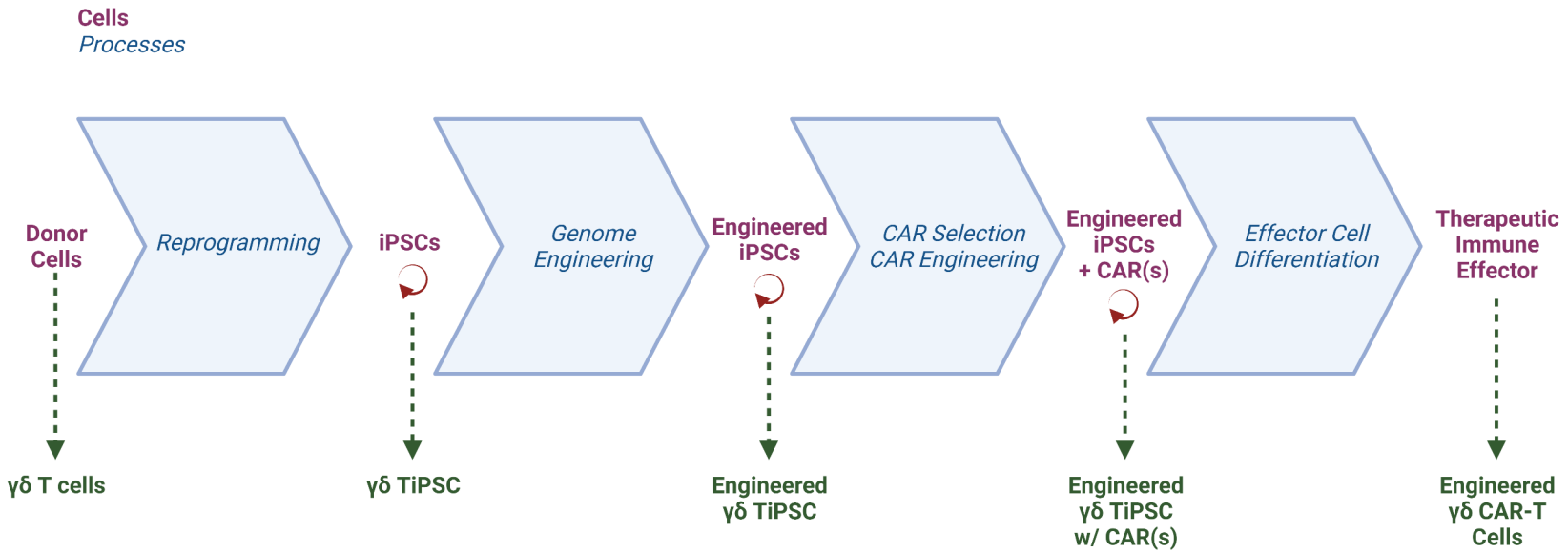
γδ T Cell Platform

Mark Wallet, PhD I VP Immuno-Oncology

iPSC-derived Therapeutics are Developed from Unique Cells and Processes

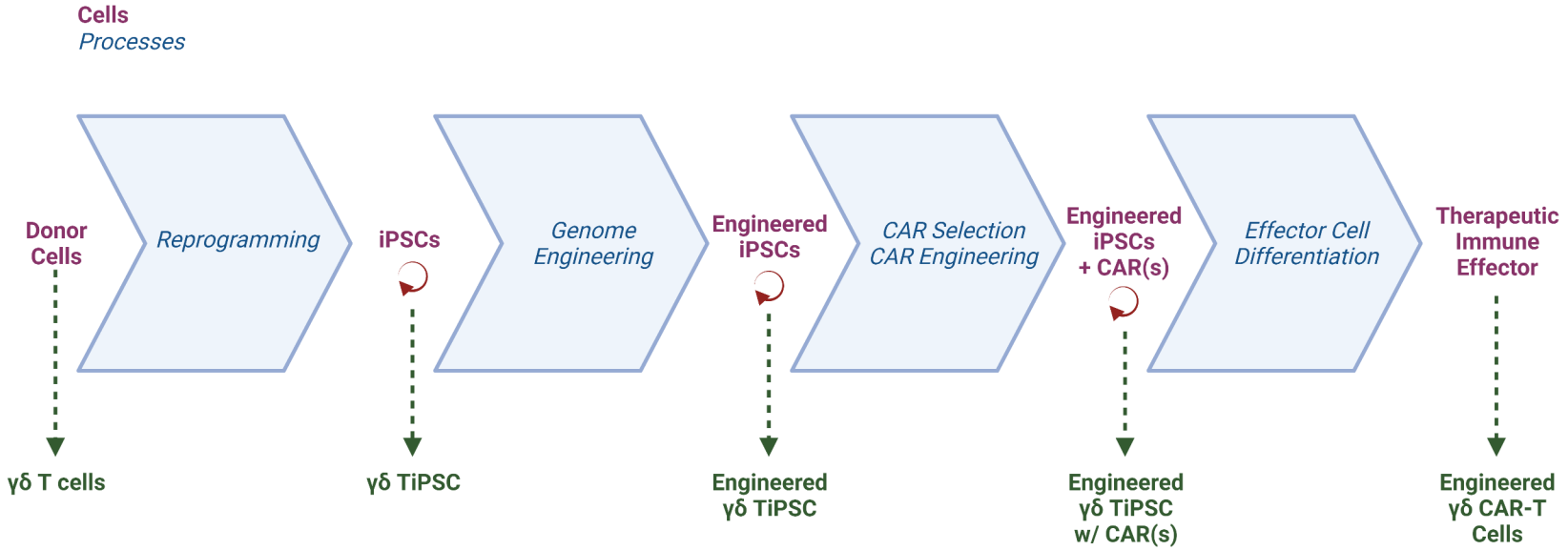


iPSC-derived Therapeutics are Developed from Unique Cells and Processes



iPSC-derived T cells

iPSC-derived Therapeutics are Developed from Unique Cells and Processes



iPSC-derived T cells

Today's update on T cell platform:

1. Reprogramming γδ T cells into TiPSC

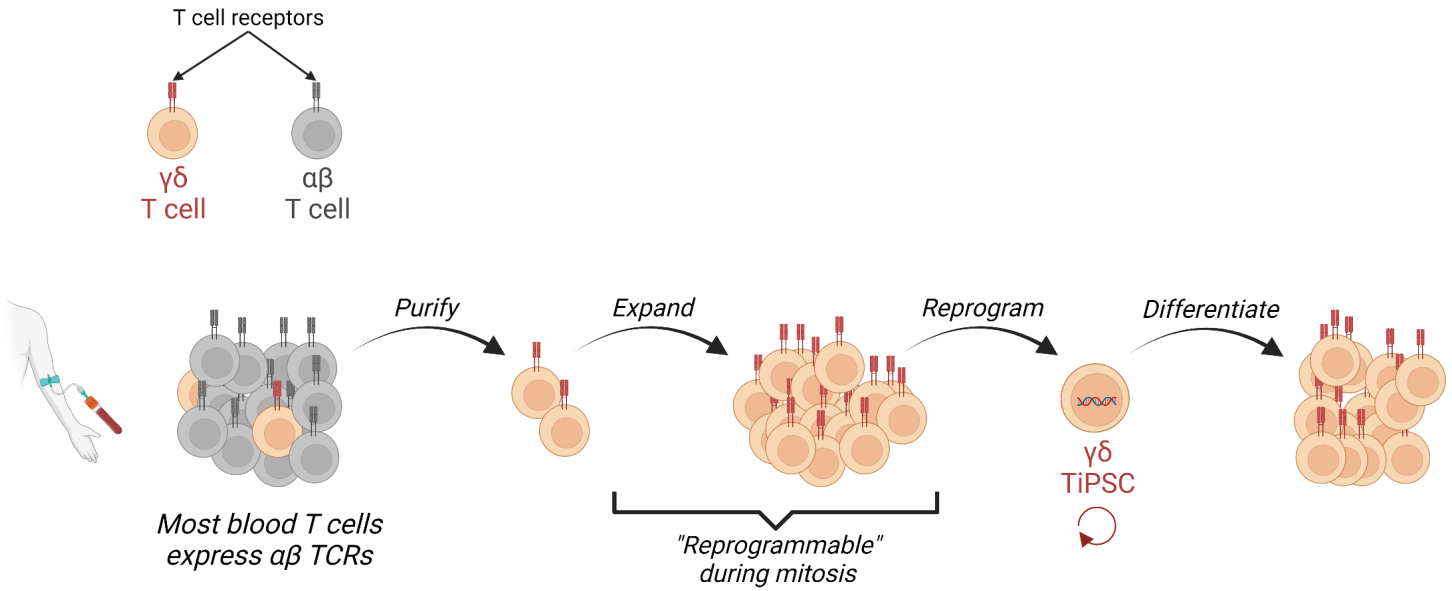
2. Engineering TiPSC for enhanced fitness

3. Differentiation of TiPSC into high-yield, high-purity γδ CAR-T cells

4. Pre-clinical studies exhibiting potent activity of γδ CAR-T cells against solid tumors

5. Leveraging Century's T cell platform for CNTY-107 [Luis Borges, CSO]

1. Reprogramming γδ T cells into TiPSC



Single blood donation enables development an entire platform with multiple products

Banked cells from healthy donors

Dozens of TiPSC lines for clinical use

Vγ9/Vδ1
Vγ9/Vδ2

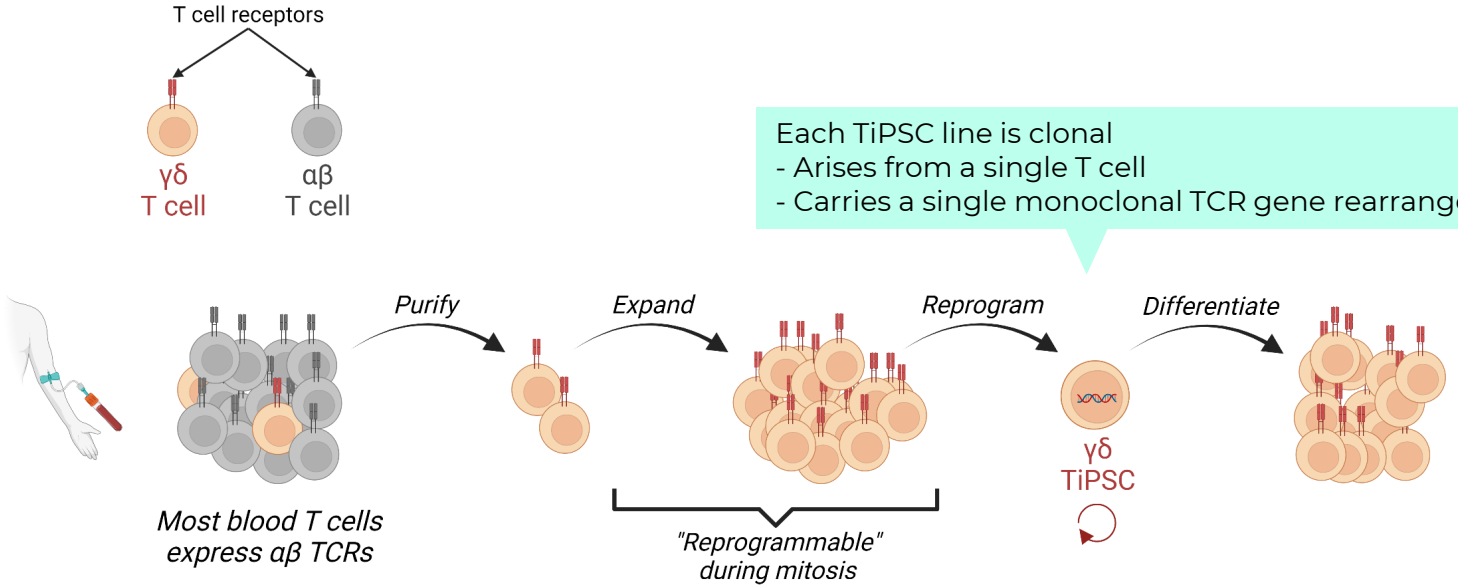
Screened for T cell differentiation and function

Narrowed to two lead lines for initial clinical programs

Vγ9/Vδ1

TCRs sequenced, cloned, and tested for allo-reactivity

1. Reprogramming γδ T cells into TiPSC



Each TiPSC line is clonal
- Arises from a single T cell
- Carries a single monoclonal TCR gene rearrangement

Single blood donation enables development an entire platform with multiple products

Banked cells from healthy donors

Dozens of TiPSC lines for clinical use

Vγ9/Vδ1
Vγ9/Vδ2

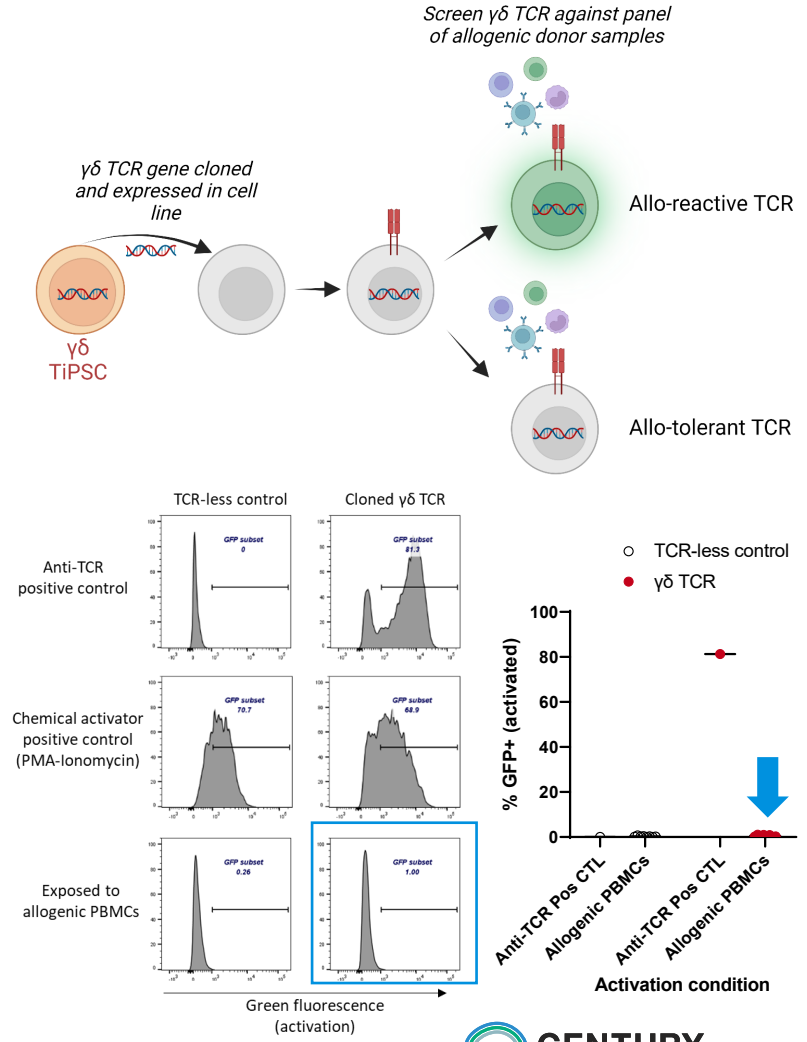
Screened for T cell differentiation and function

Narrowed to two lead lines for initial clinical programs

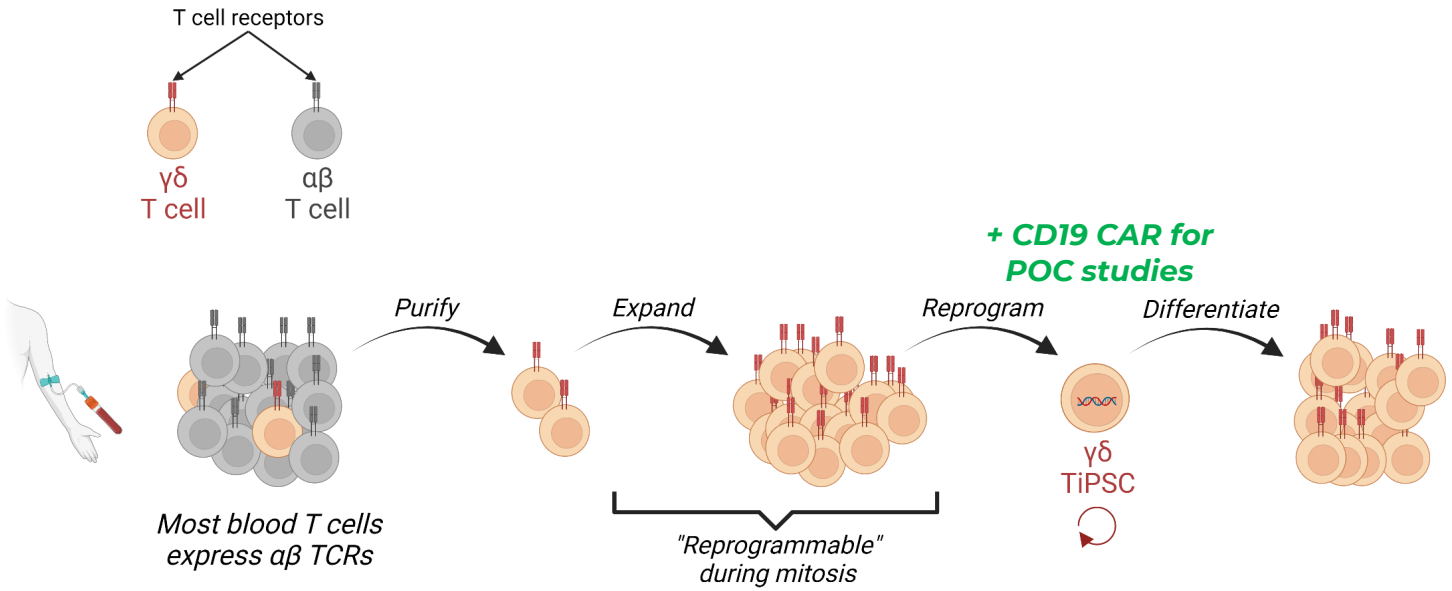
Vγ9/Vδ1

TCRs sequenced, cloned, and tested for allo-reactivity

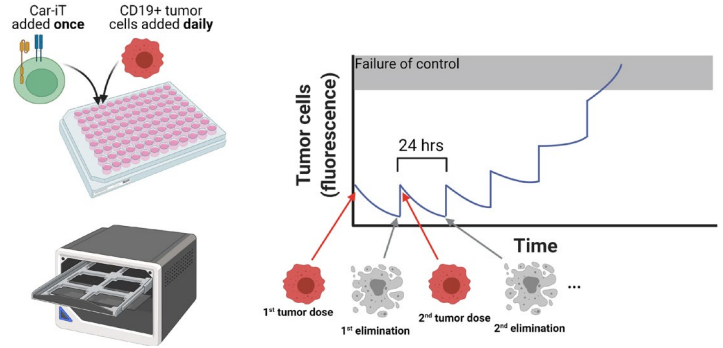
Lead γδ TCR lacks allo-reactivity

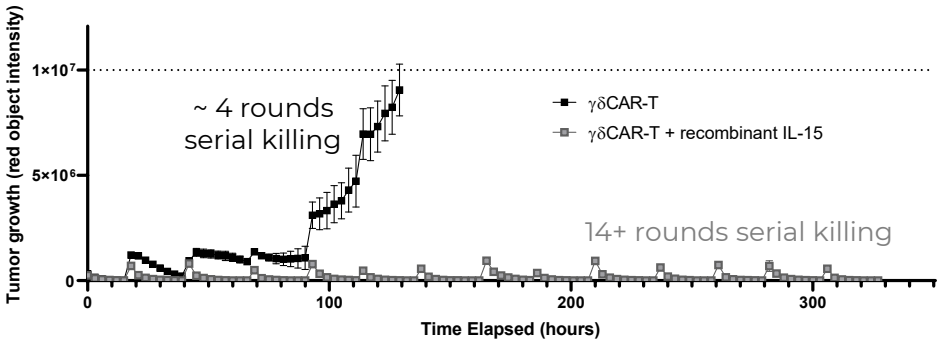


2. Engineering TiPSC for Enhanced Fitness

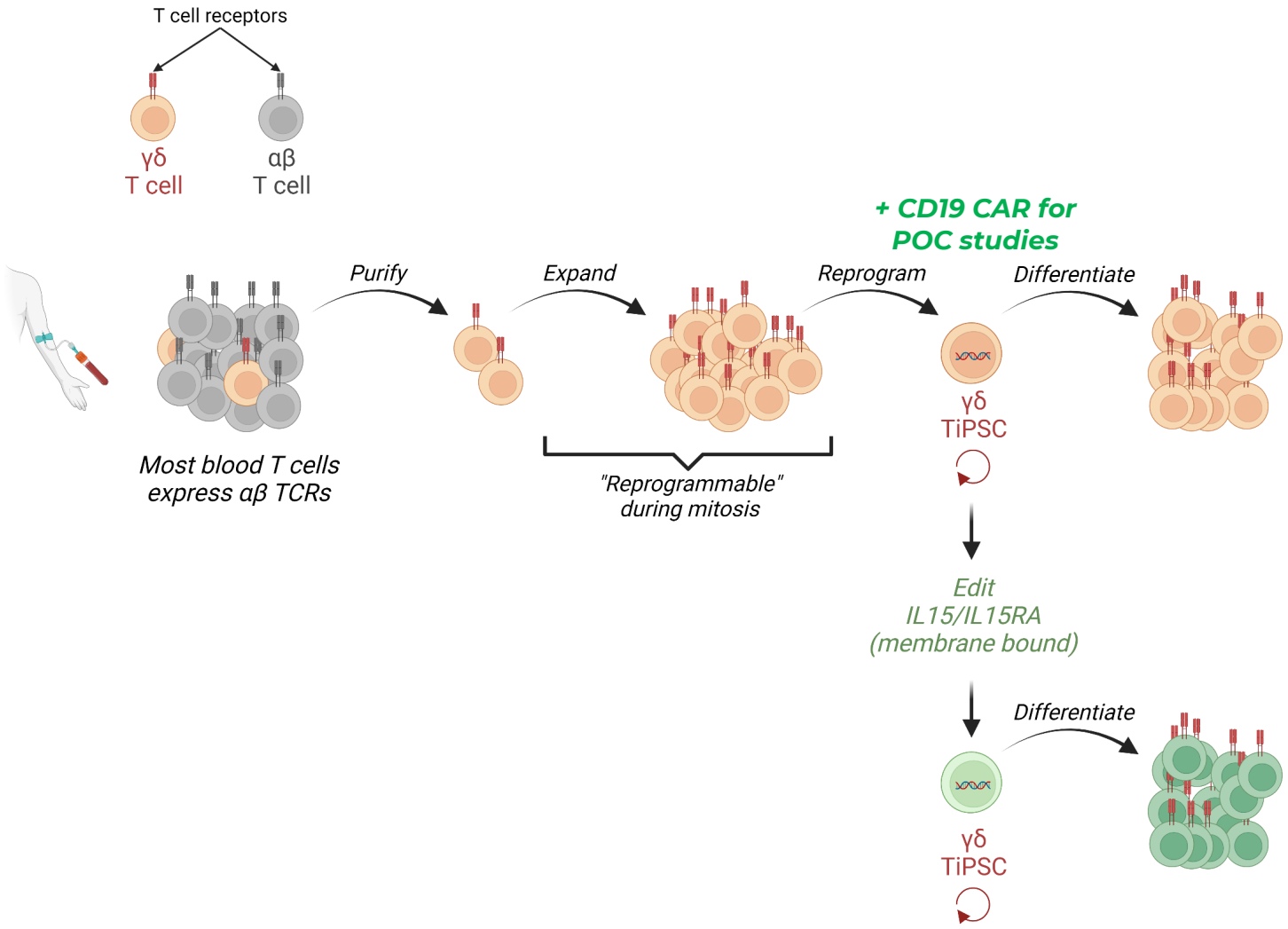


Sustained serial killing in presence of recombinant IL-15

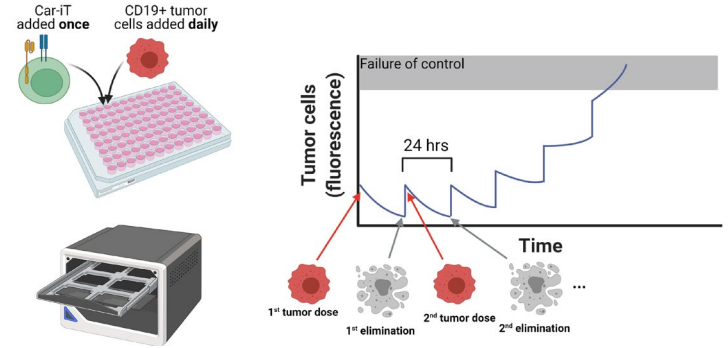


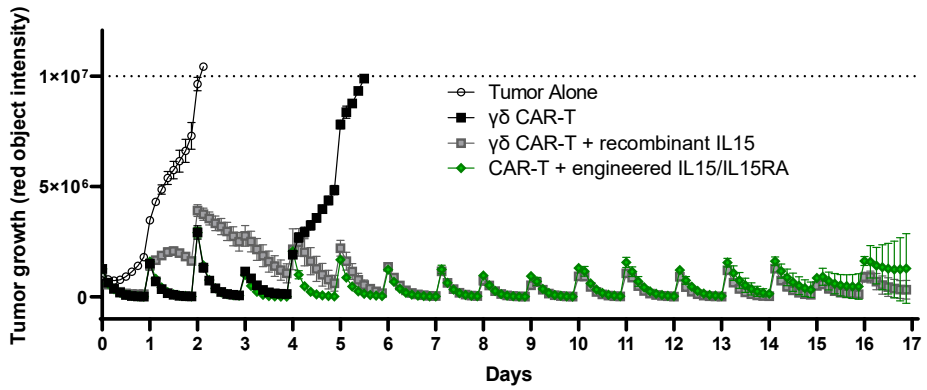


2. Engineering TiPSC for Enhanced Fitness

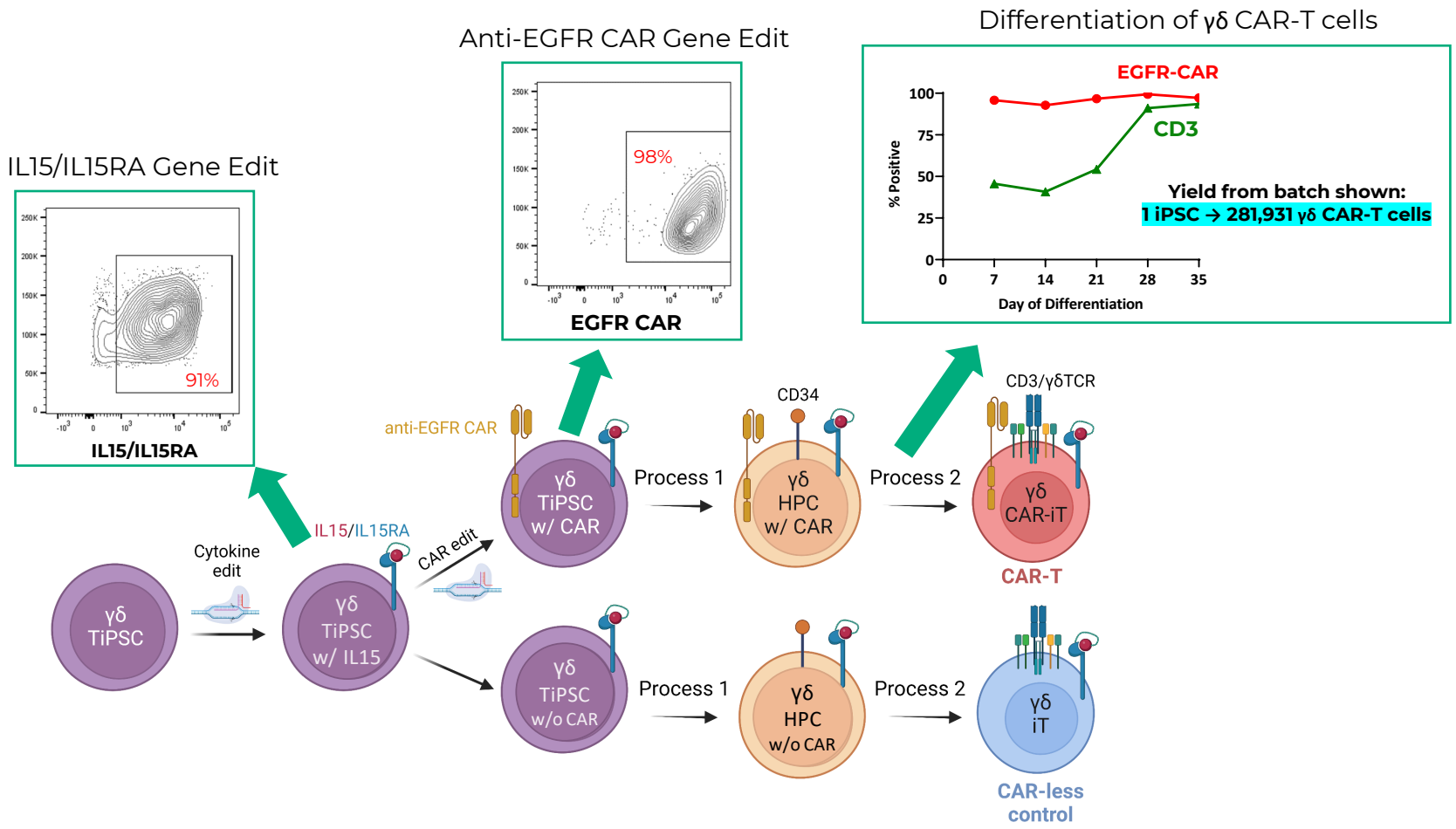


Sustained serial killing with engineered IL15/IL15RA



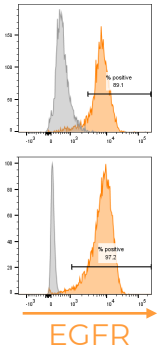


3. Differentiation of TiPSC into High-yield / High-purity T cells

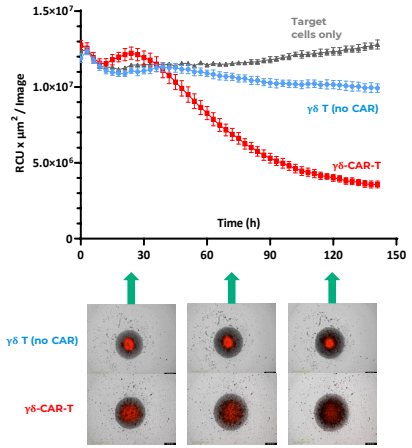


4. Preclinical Studies Exhibiting Potent Activity of γδ CAR-T Cells Against Solid Tumors

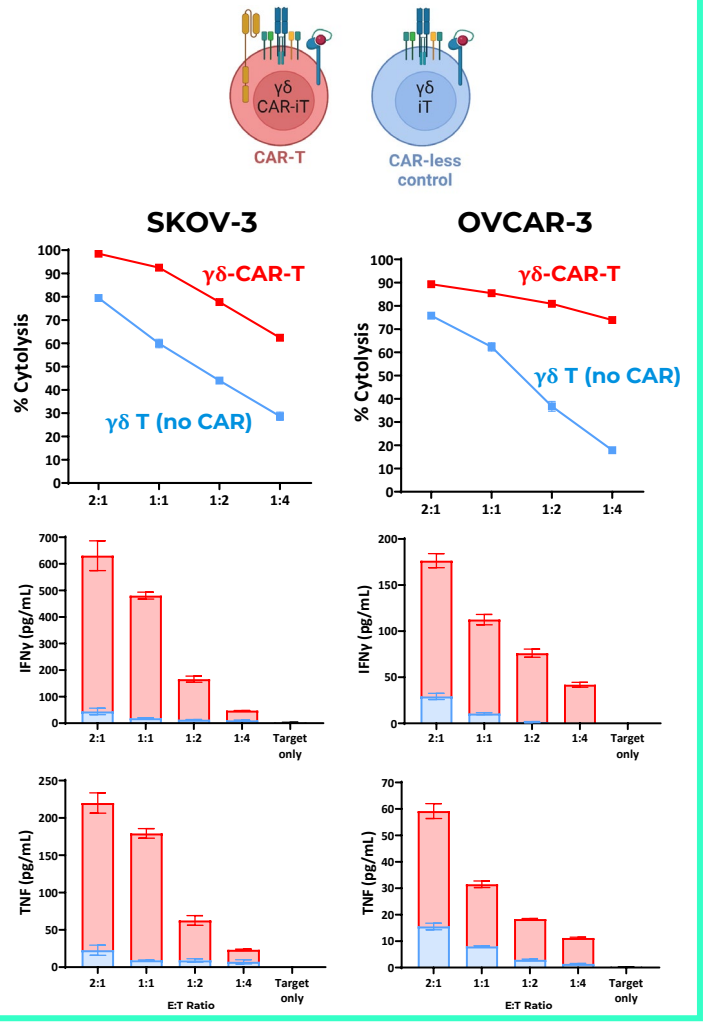
Solid Tumor Models (Ovarian)



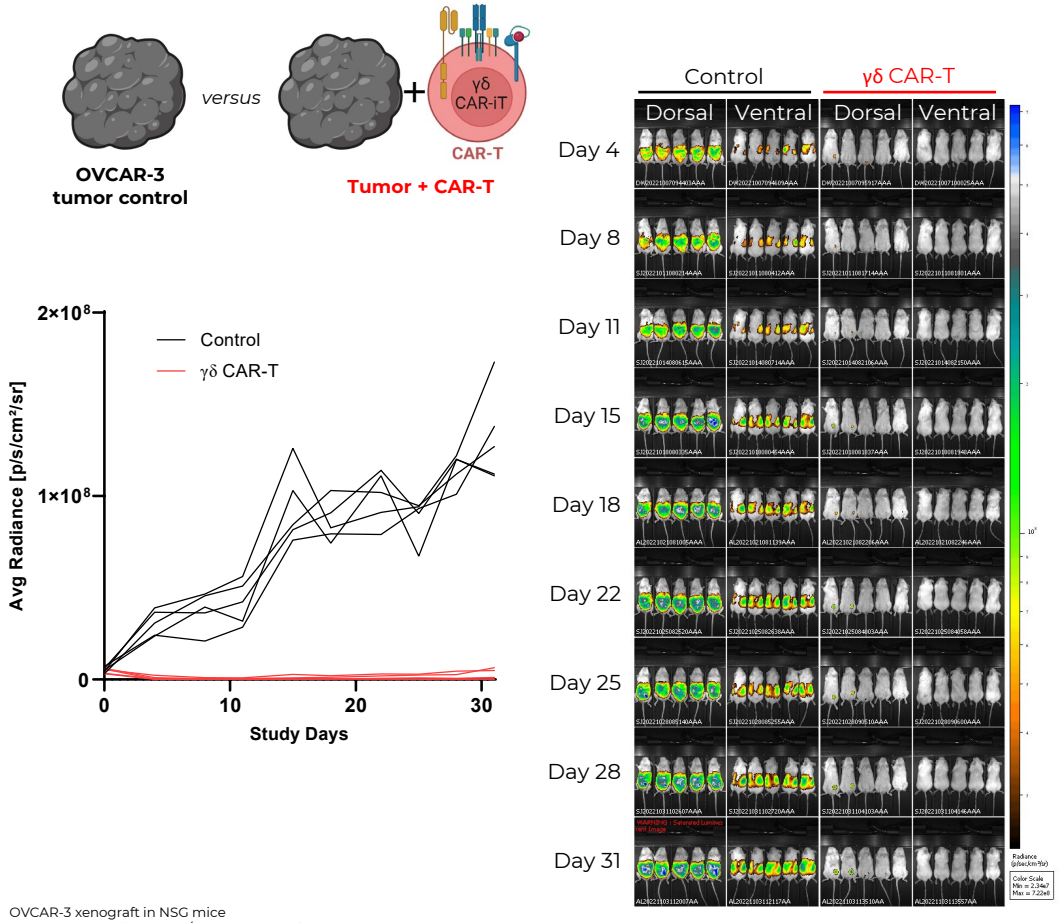
CAR-mediated killing of OVCAR-3 3D spheroids



CAR-mediated killing of solid tumor monolayers



iPSC-derived γδ CAR-T cells control ovarian cancer *in vivo*



OVCAR-3 xenograft in NSG mice
10e6 EGFR-specific IL-15RA/IL-15 engineered CAR-T

Summary

- Century has developed a fully in-house iPSC-derived γδ T cell platform
- Technical advances have enabled successful proof of concept for pre-clinical utility of γδ CAR-T cells for solid tumors
- The team is well-positioned to develop a solid tumor program for the clinic

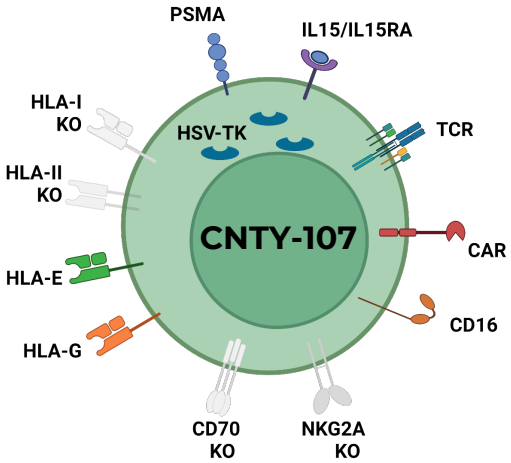
CENTURY THERAPEUTICS

CNTY-107, our γδ iT Product Candidate for the Treatment of Solid Tumors Expressing Nectin-4

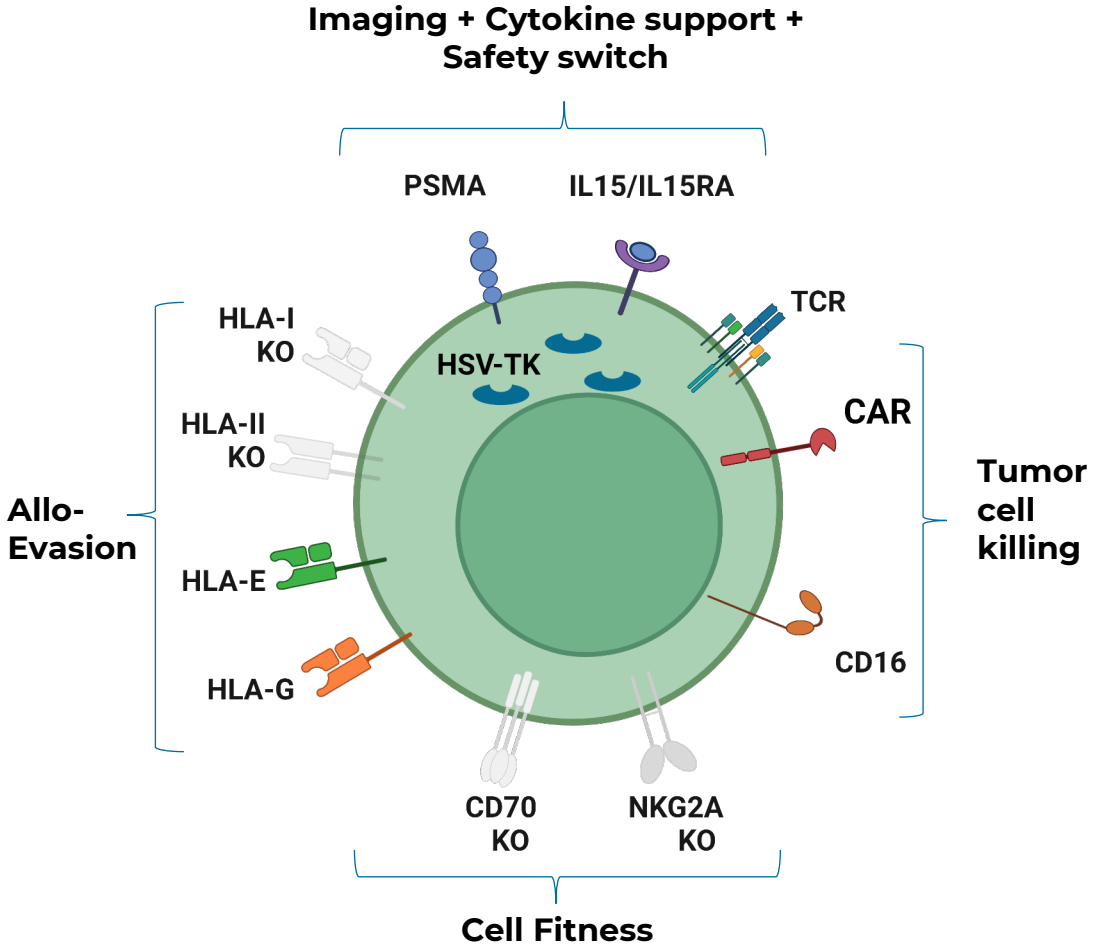
Luis Borges, PhD I CSO

CNTY-107, Next-Generation Product Candidate For The Treatment Of Nectin-4 Expressing Cancers

Challenges	Century's Solution	CNTY-107
Trafficking and infiltration	γδ iT cells - tissue homing	$\gamma_9\delta_1$ iT cells, subset of γδ T cells that preferentially home to tissues
Sufficient homeostatic cytokine support for enhanced persistence	Novel conditioning regimens Engineering	Cells engineered with homeostatic cytokine IL15/IL15Rα and Allo-Evasion™
Tumor heterogeneity	Engage innate, endogenous immunity Multi tumor targeting pathways	Three major pathways for tumor targeting: Nectin-4 CAR, CD16, and innate receptors
TME / Immunosuppressive environment	Future engineering strategies	CD16 helps maximize combinations with antibodies that modulate TME

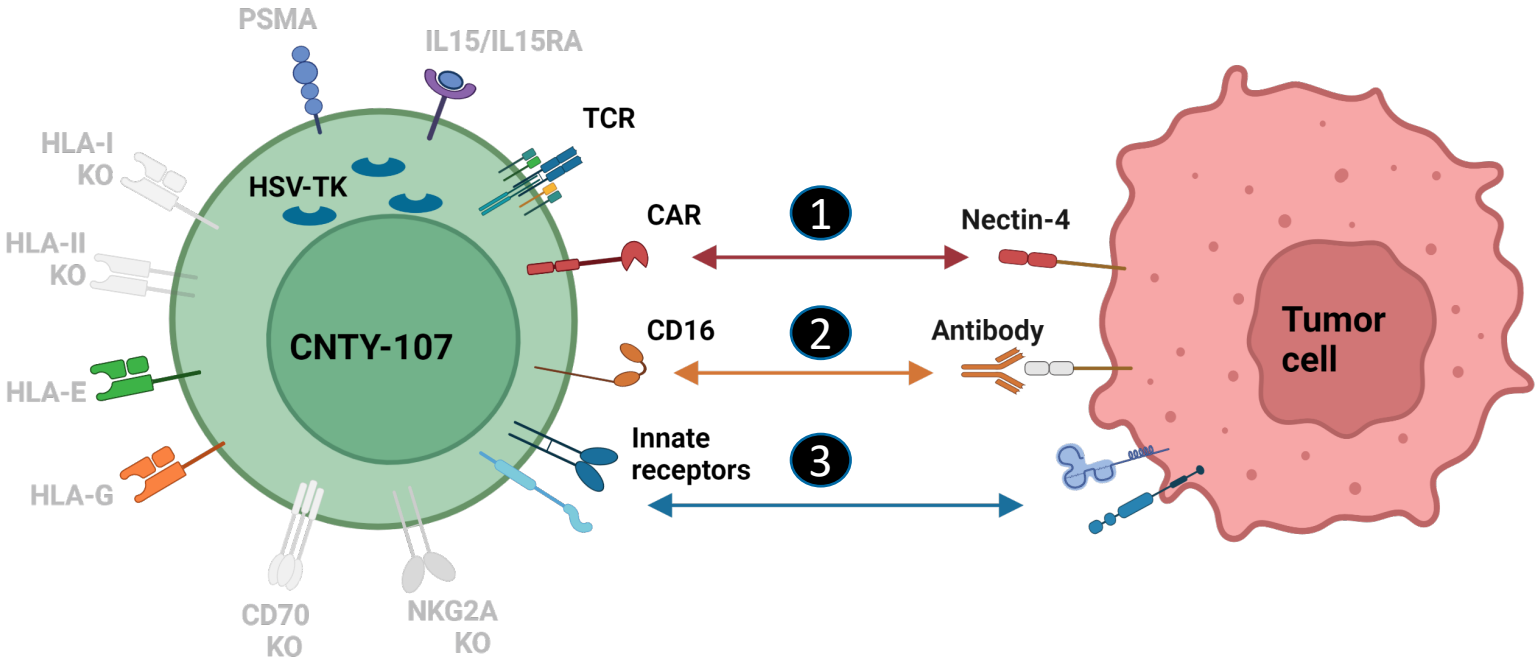


Engineering Profile of CNTY-107



ENGINEERING PROFILE			
Step	**Gene Edit**		**Rationale**
1	KO	β2M	Allo-Evasion
	KI	HLA-E-2A-HLA-G	Allo-Evasion
2	KO	NKG2A	KO landing pad, potential to block inhibitory signal
	KI	IL15/IL15Rα	Homeostatic cytokine support
3	KO	CD70	KO landing pad, potential to increase cell fitness
	KI	CD16	Tumor killing through ADCC
4	SHL	CLYBL	Safe harbor locus (SHL)
	KI	PSMA+HSV-TK	PSMA for cell tracing, HSV-TK as a safety switch
5	SHL	AAVS1	Safe harbor site
	KI	Nectin-4 -CAR	Tumor targeting
6	KO	CIITA	Allo-Evasion

CNTY-107 Has Multiple Built-In Mechanisms for Tumor Killing



PATHWAYS FOR TUMOR KILLING

1. CAR-mediated killing
2. ADCC (Antibody-dependent cellular cytotoxicity)
3. Innate receptors (NCRs, others) mediated killing though recognition of stress ligands

Nectins

Nectins are cell adhesion molecules (CAMs) involved in Ca^{2+}-independent cell-cell interactions

The Nectin family includes four Nectins

- Nectins 1-3 are enriched in normal adult tissues
- Nectin-4 is mostly expressed during fetal development and its expression declines in adult tissues (low expression levels in skin, bladder, placenta, oral mucosa, and tonsils)

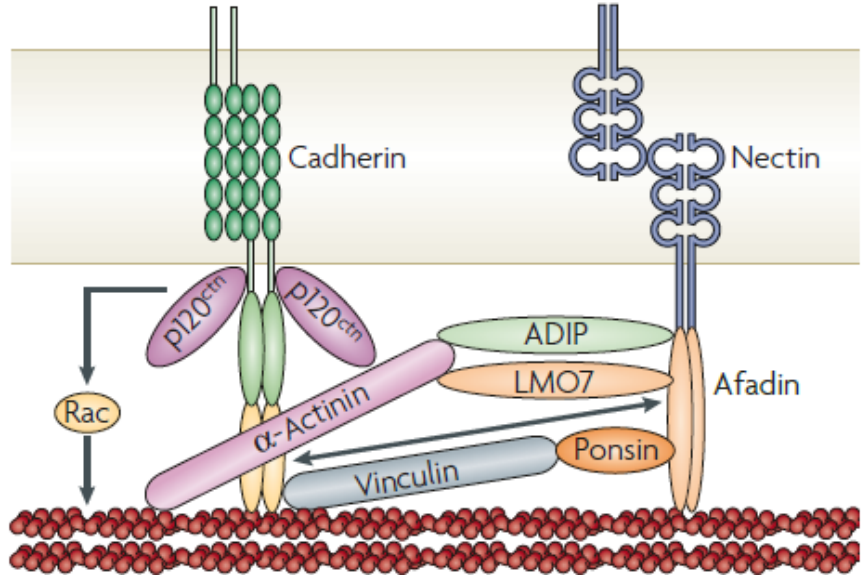
Nectins interact with other cell surface molecules including cadherins, integrins and growth factor receptors

- These interactions help modulate cell adhesion, migration, and proliferation

Nectin-4 dimers bind to Nectin-1 or Nectin-4 on adjacent cells

Nectin-4 also binds TIGIT on immune cells and this interaction leads to inhibition of NK cells

Interactions of Nectins and Cadherins Interact to Form Adherens Junctions and Promote Cell Adhesion



Adherens junction

Figure adapted from Takai et al, Nat Rev Mol Cell Biol, 2008

Nectin-4 Expression in Cancer

- Nectin-4 is expressed in high frequency in bladder, breast, lung, pancreatic, ovarian, head & neck, and esophageal cancers
- The highest levels of expression of Nectin-4 are seen in bladder, breast, lung and pancreatic cancers
- Clinical validation of Nectin-4 as a tumor target has been demonstrated by the approval Enfortumab vedotin for the treatment of urothelial cancer

IHC Analysis of the Expression of Nectin-4 in a Panel of 2,394 Human Tumor Specimens

	Intensity of staining[a]				
Cancer type	Strong N (%)	Moderate N (%)	Low N (%)	Negative N (%)	Overall positive (%)
Bladder (N = 524)	162 (31)	154 (29)	118 (23)	90 (17)	
Transitional (N = 467)	(34)	(30)	(21)	(16)	83
Metastasis (N = 25)	(12)	(44)	(36)	(8)	
Others (N = 32)	(6)	(16)	(31)	(47)	
Breast (N = 654)	174 (27)	168 (26)	170 (26)	142 (22)	
Ductal carcinoma (N = 386)	(31)	(25)	(23)	(21)	
Lobular carcinoma (N = 30)	(20)	(27)	(33)	(20)	78
Metastasis (N = 203)	(18)	(27)	(31)	(24)	
Others (N = 35)	(31)	(26)	(23)	(20)	
Pancreatic (N = 164)	21 (13)	39 (24)	56 (34)	48 (29)	71
Lung (N = 618)	46 (7)	121 (20)	173 (28)	278 (45)	
Squamous (N = 235)	(10)	(22)	(30)	(38)	
Adenocarcinoma (N = 212)	(5)	(25)	(34)	(36)	
Small cell carcinoma (N = 50)	(0)	(0)	(2)	(98)	55
Metastasis (N = 77)	(12)	(19)	(29)	(40)	
Others (N = 44)	(7)	(5)	(18)	(70)	
Ovarian (N = 118)	0	21 (18)	46 (39)	51 (43)	
Serous (N = 60)	0	(2)	(45)	(53)	
Mucinous (N = 14)	0	(50)	(7)	(43)	57
Metastasis (N = 40)	0	(32)	(45)	(23)	
Others (N = 4)	0	(0)	(0)	(100)	
Head & Neck (N = 135)	3 (2)	22 (16)	54 (40)	56 (41)	59
Esophageal (N = 181)	7 (4)	37 (20)	55 (30)	82 (45)	55
Total (N = 2,394)	413 (17)	562 (24)	672 (28)	747 (31)	69

[a]Intensity of staining: strong, H-score = 200–300; moderate, H-score = 100–199; low, H-score = 15–99; negative, H-score = 0–14.

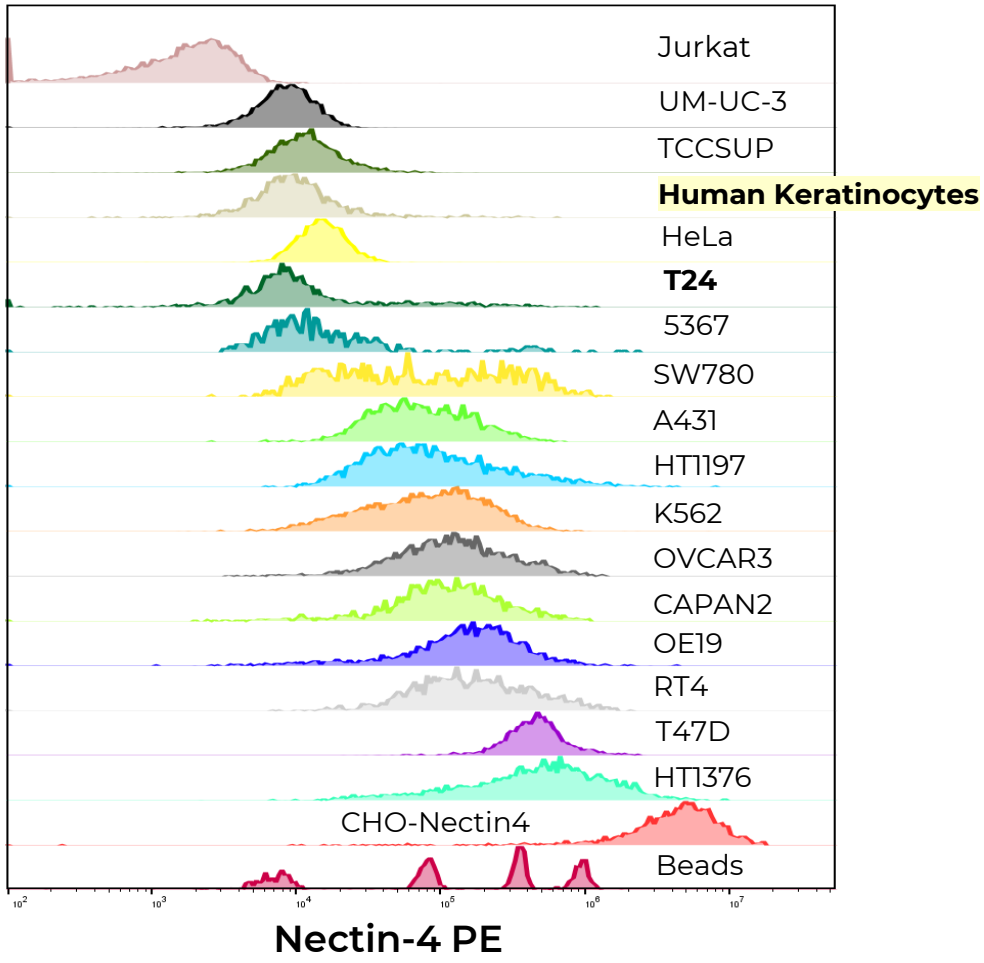
From Challita-Eid et al., Cancer Research, 2016

Tumors With the Highest Expression of Nectin-4

Tumor Histology	Moderate to High Expression
Bladder	60%
Breast	53%
Pancreatic	37%
Lung	27%

Nectin-4 Expression Levels On Human Skin Keratinocytes Is Lower Than In Most Tumor Cell Lines

Nectin-4 Expression in Multiple Cells

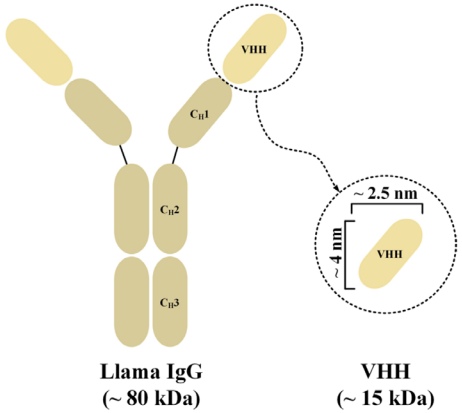


Ranking Of Tumor Cells Based On Nectin-4 Expression Level

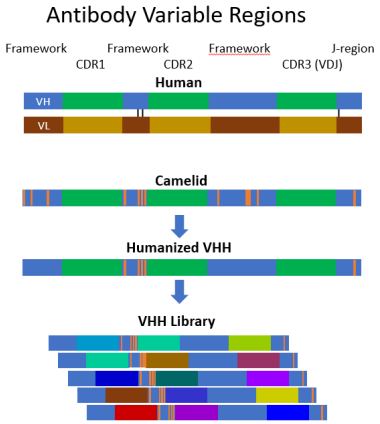
Cell Line	Origin	Ranking
UM-UC-3	Bladder cancer	Negative
TCCSUP	Bladder cancer	
JURKAT	T cell	
HeLa	Cervical cancer	
T24	Bladder cancer	Low (50-250)
Human keratinocytes	**Normal skin**	
5637	Bladder cancer	
HT1197	Bladder cancer	Medium (3,000 - 10,000)
SW780	Bladder cancer	
K562	CML	
A431	Breast cancer	
CAPAN2	Pancreatic cancer	
OVCAR3	Ovarian cancer	
OE19	Esophageal cancer	
RT4	Bladder cancer	
HT1376	Bladder cancer	High (10,000+)
T47D	Breast cancer	
CHO-Nectin4	Chinese Hamster Ovary	

Selection of VHH Binders to Build Nectin-4 CAR

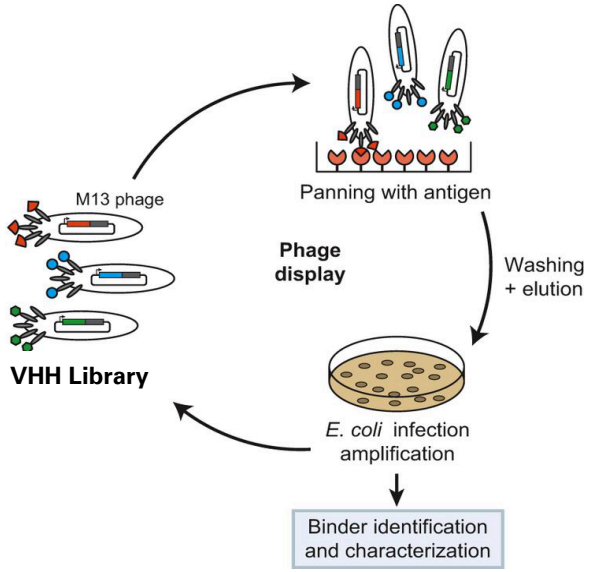
Llama VHH antibodies



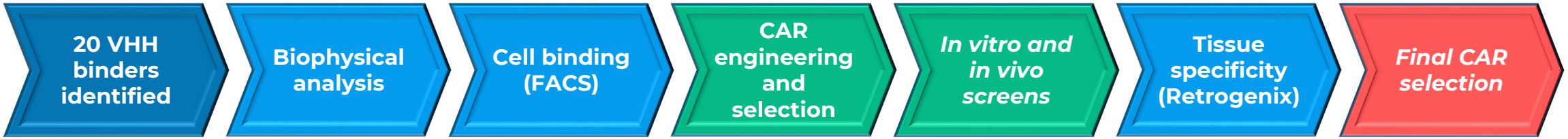
Century's Proprietary VHH Libraries



Llama VHH Library Screens

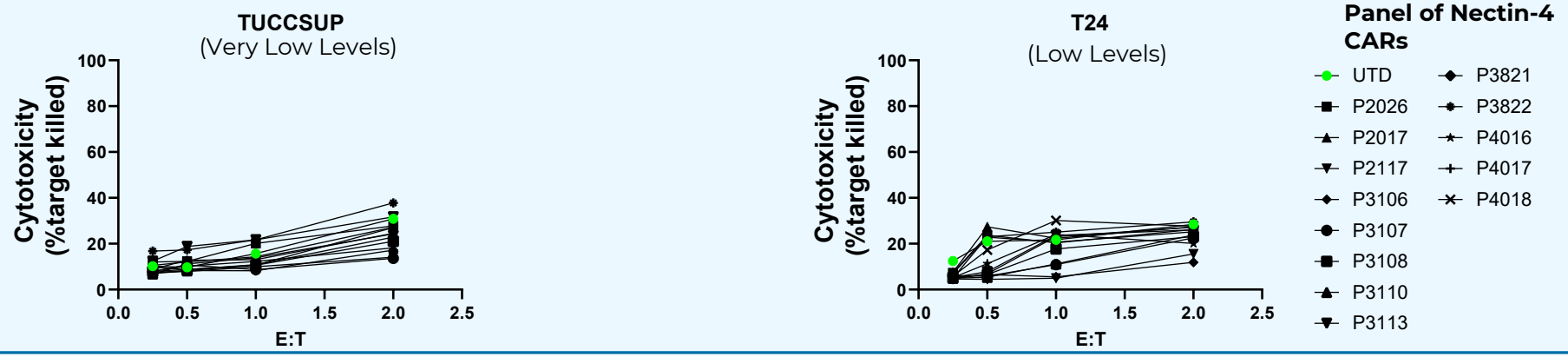


Assay Screening Flow to Select Nectin-4 Binders and CARs

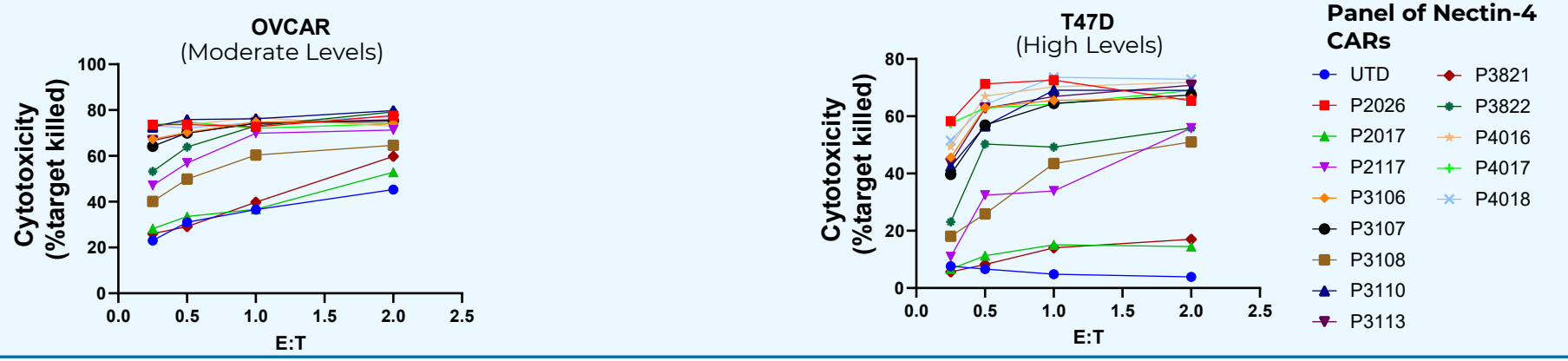


Century's Nectin-4 CARs Distinguish Between Cells Expressing Low vs. Moderate to High Levels Of Nectin-4

Century's Nectin-4 CARs Do Not Kill Cells Expressing Low Levels of Nectin-4

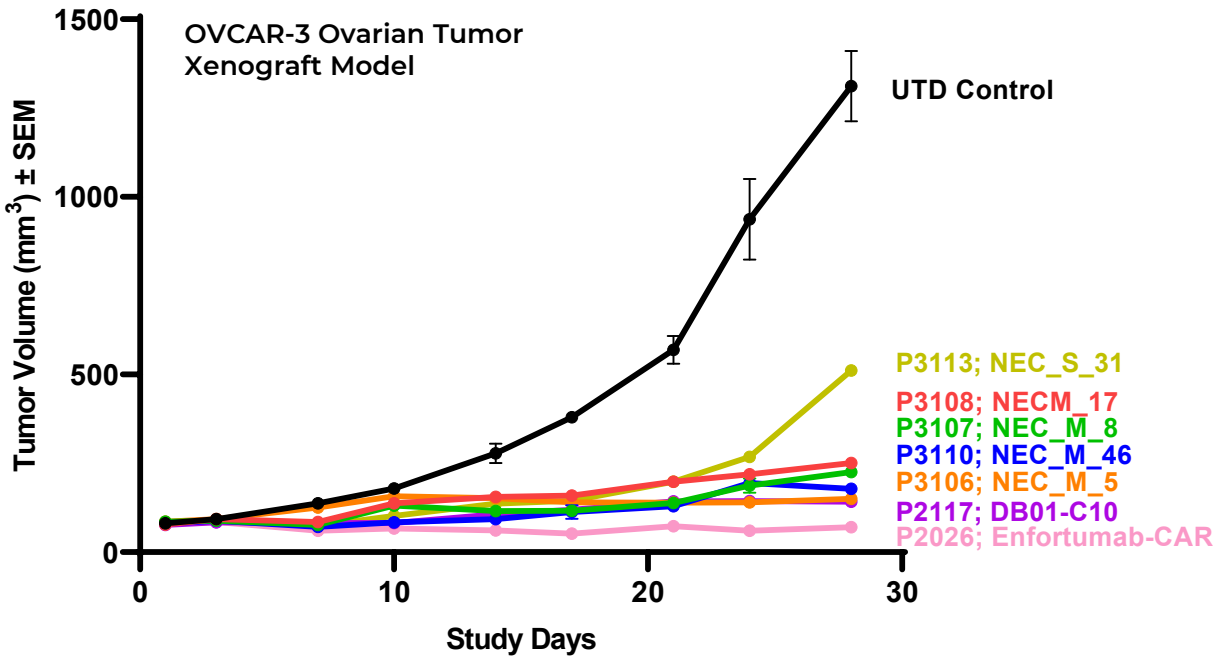


Century's Nectin-4 CARs Kill Cells Expressing Moderate to High Levels of Nectin-4



CNTY-107 Nectin-4 CARs Mediate Robust Anti-Tumor Activity *in Vivo*

In Vivo Evaluation of the Anti-tumor Activity Nectin-4 CARs Using Peripheral Blood CAR-T Cells



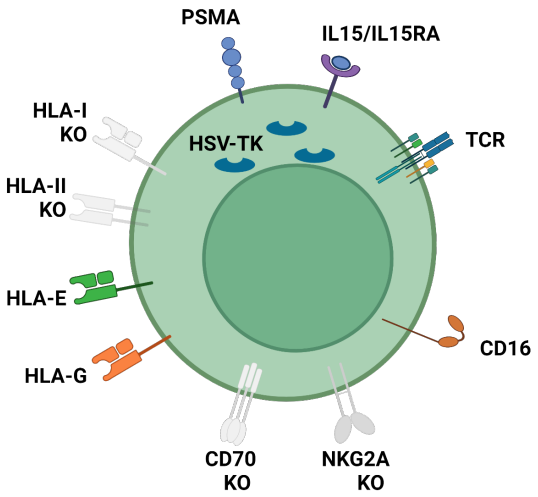
- 5x10^6 OVCAR-3 cells implanted subcutaneously in the right flank
- Mice randomized after tumors reached 75-125 mm3
- Mice treated with 5x10^6 CAR-T cells

All CAR Constructs Mediated Statistically Significant Tumor Growth Inhibition (TGI)

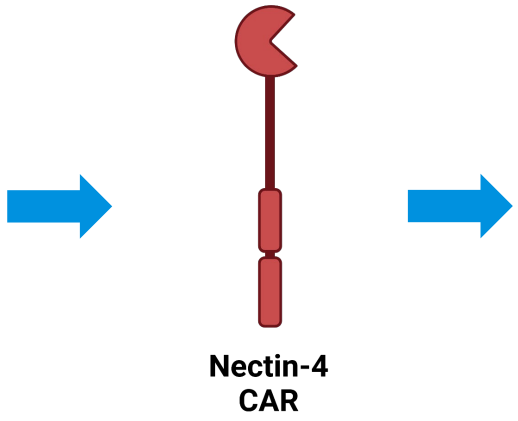
Treatment Group	Day 28 % TGI	Day 28 P-Value
P3108 - NECM_17	80.8	0.0003
P3107 - NEC_M_8	82.8	0.0002
P3110 - NEC_M_46	86.4	0.0001
P3106 - NEC_M_5	88.5	0.0001
P2117 - DB01-C10	89.2	0.0007
P3113 - NEC_S_31	61.1	0.0116
P2026 – Enfortumab-CAR	94.7	<0.0001

CNTY-107 Next Steps and Milestones

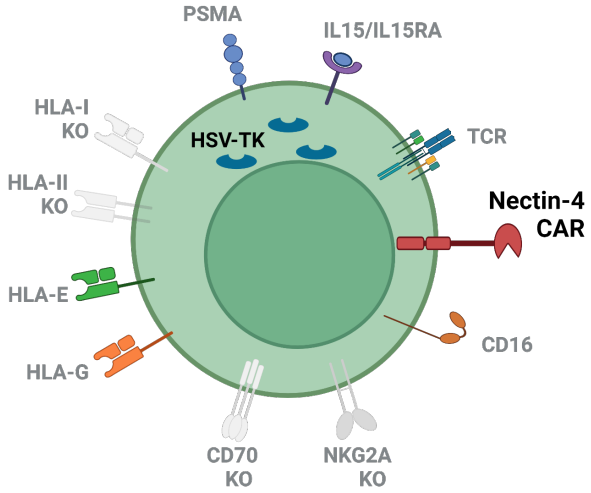
Complete Engineering of the γδ iT Common Progenitor



Select Nectin-4 CAR



Add CAR to γδ iT CP to Generate CNTY-107



Major CNTY-107 Product Candidate Milestones

Completion of CNTY-107 Engineering	Clinical Candidate Selection	IND Filing
1H23	2H23	2025

CNTY-107 Preliminary Clinical Strategy

- **Initial Phase I clinical study is planned to be run as a basket trial that will include multiple Nectin-4 positive cancers**
  - Cancers under consideration include bladder, breast, pancreatic, non-small cell lung cancer, esophageal, head and neck, and/or ovarian cancers
- **Dose-escalation will be done in the basket trial**
- **The clinical trial will be designed to expand in any indication with acceptable tox and clinical responses**
- **To enrich for potential responders among selected indications, we are developing an IHC-based Nectin-4 screening assay to potentially help select patients**
  - We will develop our own fit-for-trial IHC assay
- **Ability to evaluate combination therapies**
  - Combination therapy cohorts could be indication-specific (e.g., HER-2 antibody for breast cancer) or "generic", addressing modulation of the TME (e.g., PD-L1 antibody, Avelumab)

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Thank you

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Q&A