MiNK Therapeutics

R&D DAY

November 10th, 2022

Disclaimer and Forward-Looking Statements

This presentation contains forward-looking statements that are based on management's beliefs and assumptions and on information currently available to management. All statements other than statements of historical facts contained in this presentation are forward-looking statements. Forward-looking statements include, but are not limited to, statements concerning: the therapeutic and curative potential of agenT-797 and iNKT cells, the mechanism of action, potency and safety of agenT-797 and iNKT cells, interim or top-line data, future development plans and timelines (including pre-clinical, clinical, regulatory, manufacturing and commercial),estimated treatment costs, our ability to continue to successfully manufacture iNKT cells (including capacity and scalability), and any other statements containing the words "may," "believes," "expects," "anticipates," "hopes," "intends," "plans," "forecasts," "estimates," "will" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are subject to risks and uncertainties, including the factors described under the Risk Factors section of the most recent Form 10-K, Form 10-Q and the S-1 Registration Statement filed with the SEC. Actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. There are several important factors that could cause MiNK's actual results to differ materially from those indicated by such forward-looking statements, including a deterioration in MiNK's business or prospects; adverse developments in clinical development, including unexpected safety issues observed during a clinical trial; adverse developments in the U.S. or global capital markets, credit markets or economies generally; and changes in regulatory, social, and political conditions. For instance, actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the uncertainties inherent in the initiation, enrollment and maintenance of patients, and completion of clinical trials, availability and timing of data from ongoing clinical trials, expectations for the timing and steps required in the regulatory review process, including our ability to obtain regulatory clearance to commence clinical trials, expectations for regulatory approvals, the impact of competitive products, our ability to enter into agreements with strategic partners. When evaluating MiNK's business and prospects, careful consideration should be given to these risks and uncertainties. These statements speak only as of the date of this presentation, and MiNK undertakes no obligation to update or revise these statements.

MiNK Therapeutics

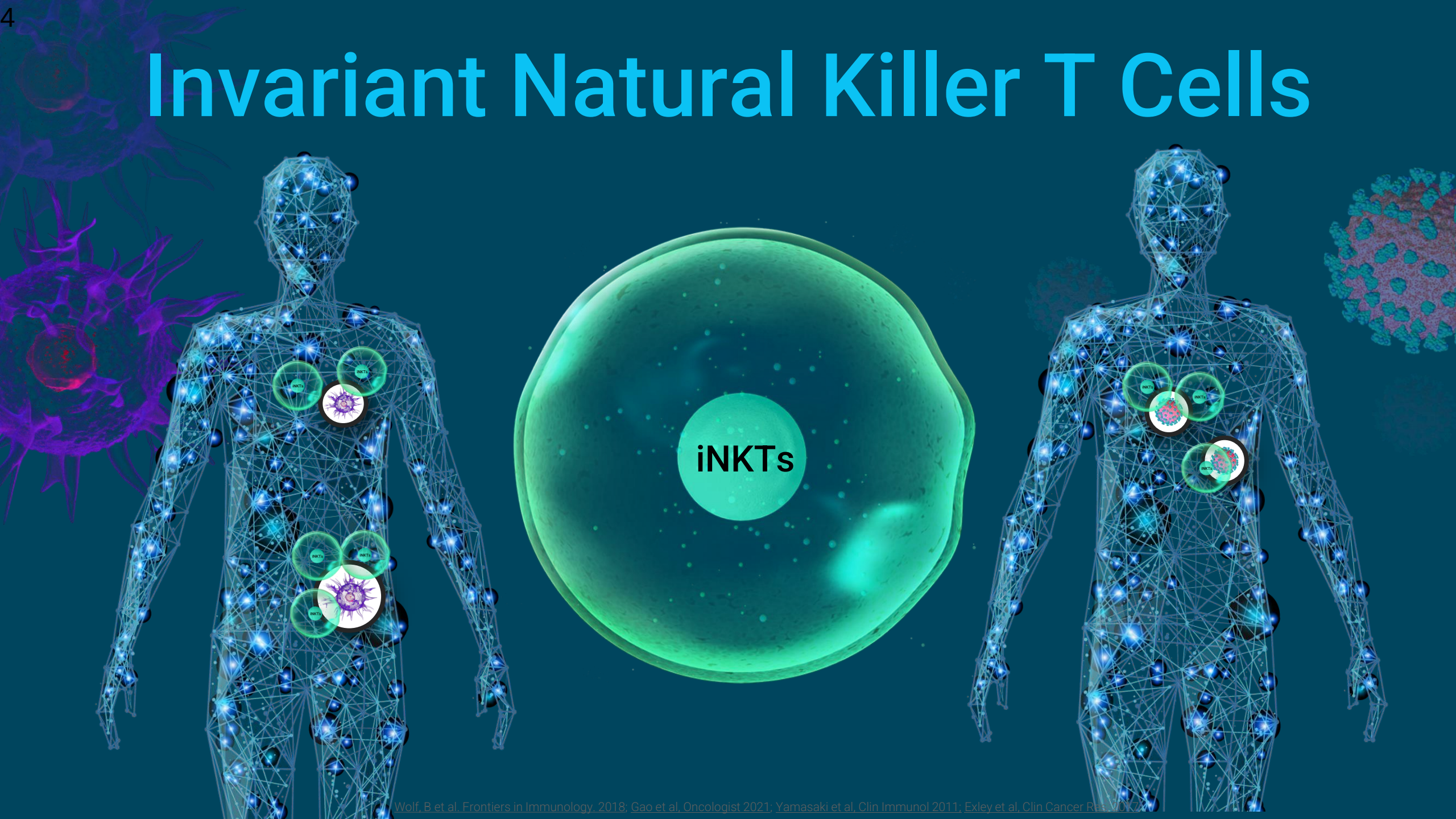
R&D DAY

Jennifer Buell, Ph.D.

President & Chief Executive Officer
MiNK Therapeutics

MiNK Therapeutics advancing novel medicines and optimal combinations that are accessible and scalable

Invariant Natural Killer T Cells

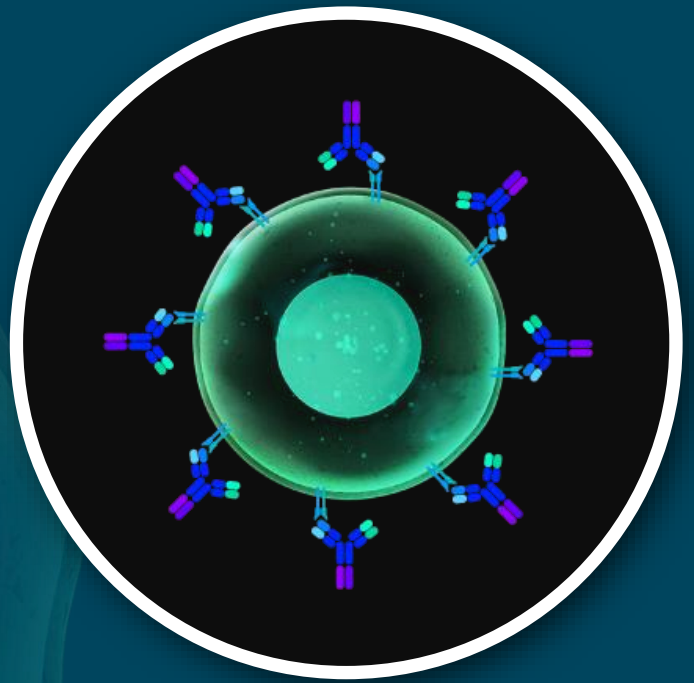


Wolf, B et al. Frontiers in Immunology. 2018; Gao et al, Oncologist 2021; Yamasaki et al, Clin Immunol 2011; Exley et al, Clin Cancer Res 2017

Draw Cells from Healthy Donors

Isolate & Expand Cells

Administer via Infusion



NewYork-Presbyterian

Weill Cornell Medicine

Dr. Manuel Hidalgo

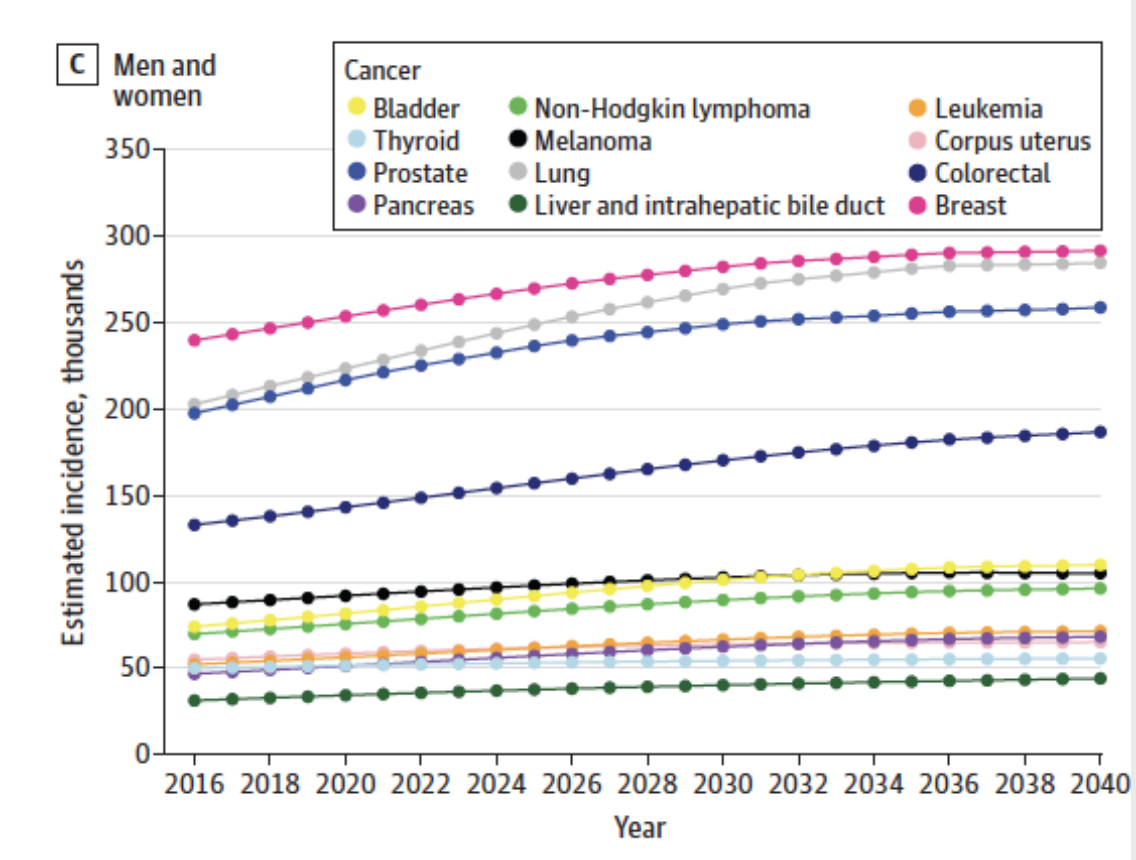
Chief of the Division of Hematology and Medical Oncology at Weill Cornell Medicine and New York-Presbyterian/Weill Cornell Medical Center

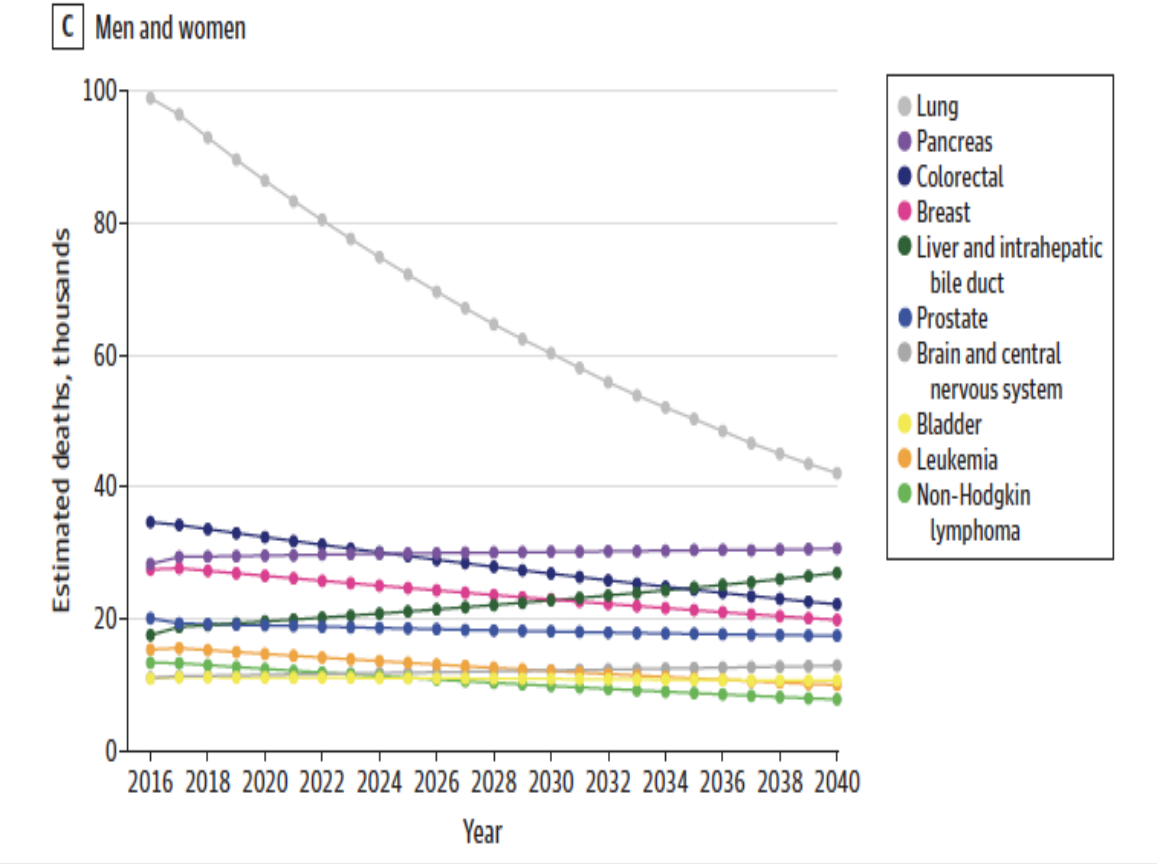
Cancer Treatment: What is Working and How Can We Improve?

COI Disclosure

- **BOD:** BMS
- **Founder:** Champions Oncology, Nelum Pharmaceuticals
- **Stock holder:** Champions Oncology, Nelum Pharmaceuticals, Highlight Therapeutics, Oncomatrix, Inxmed, BMS, Agenus
- **Research support:** PanCan, TBA alliance, Agenus, RANK Therapeutics
- **Honorarium:** MiNK, Oncomatrix, Inxmed, Fibrogen, BMS, Velavigo
- **Royalties:** Myriad, Kahr, Peaches

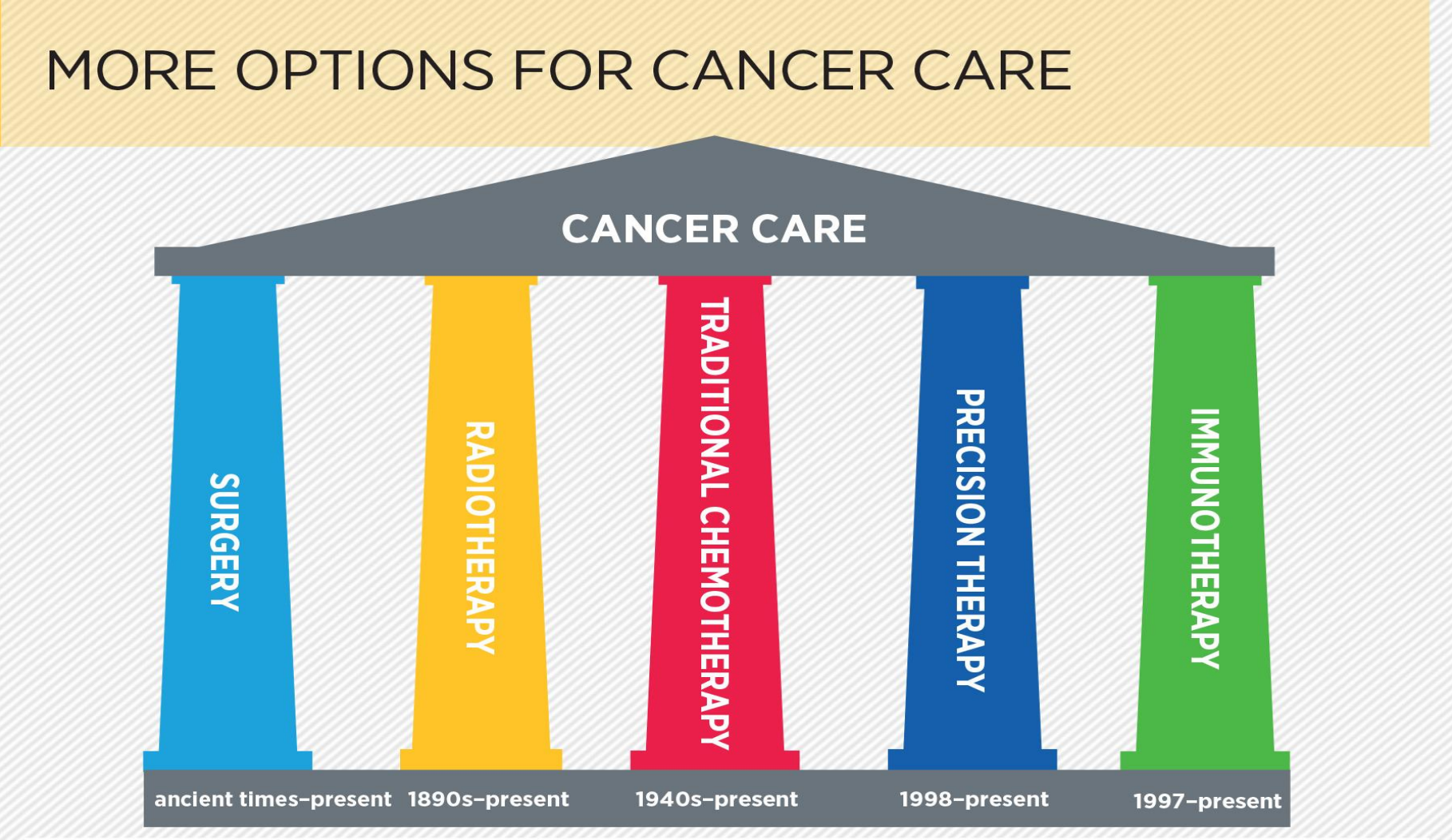
Estimated Projection Cancer Incidence and Death



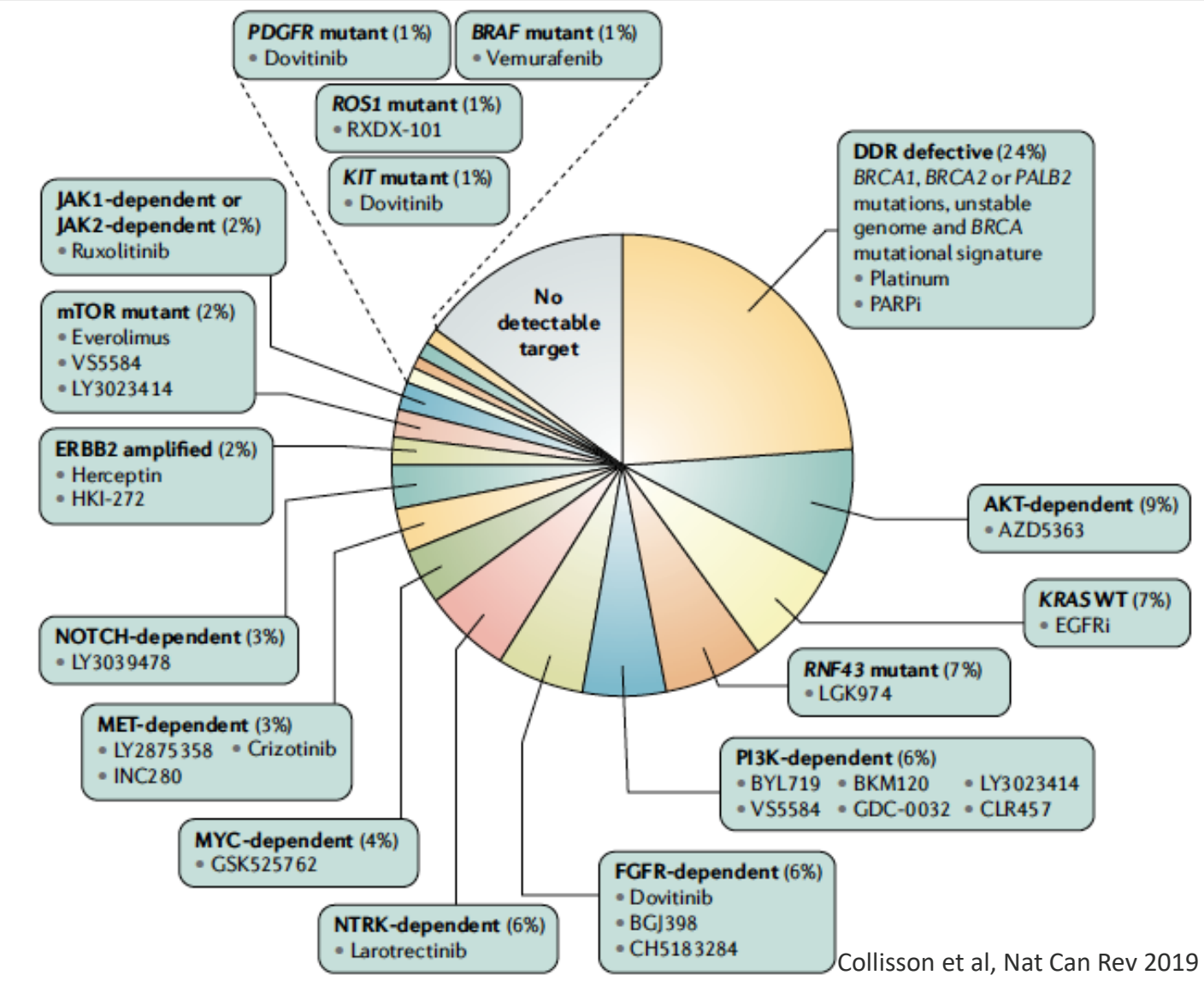


Rahib et al, JAMA Net 2021

Pillars of Cancer Care

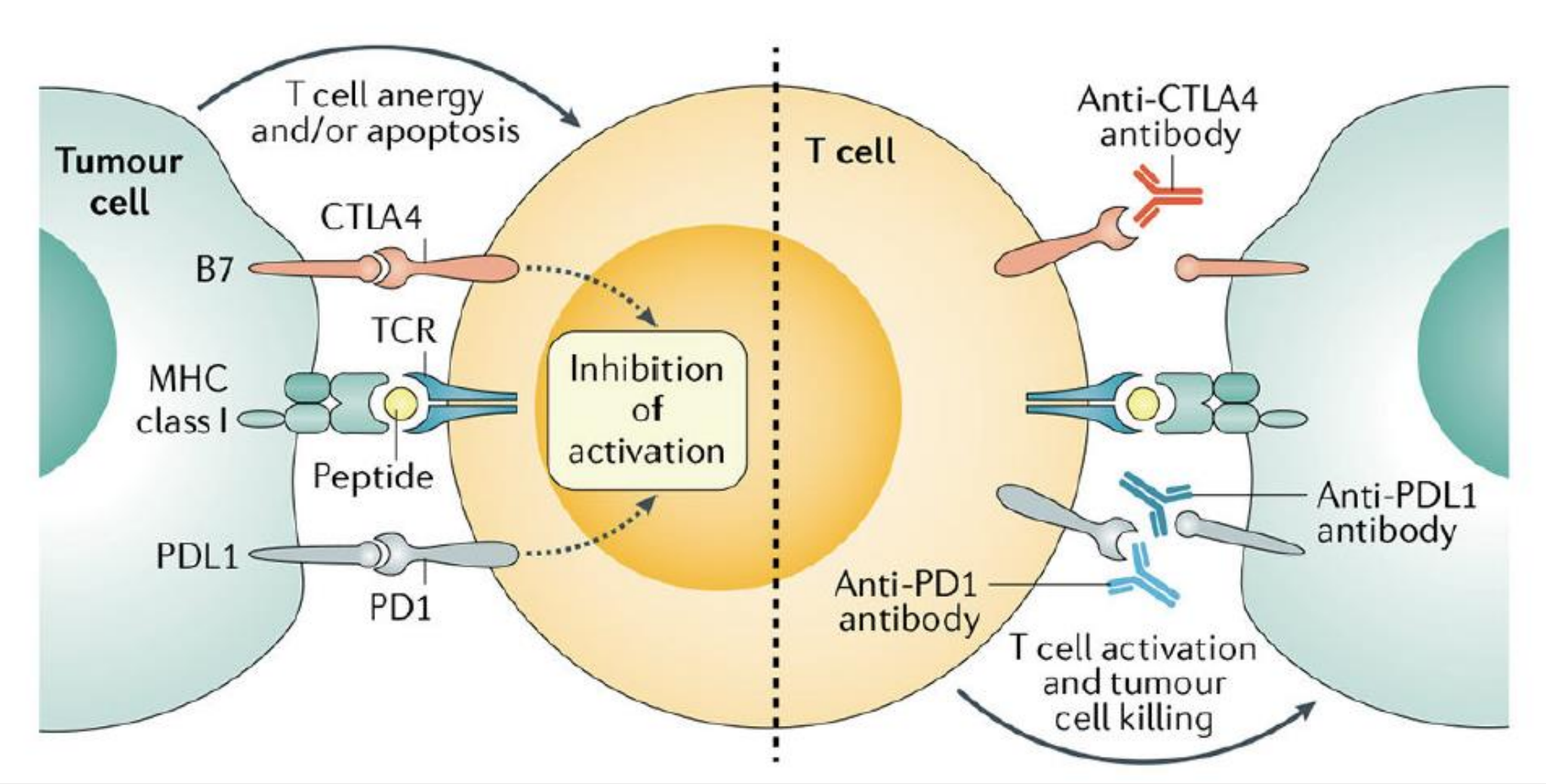


Putative Targets and Inhibitors



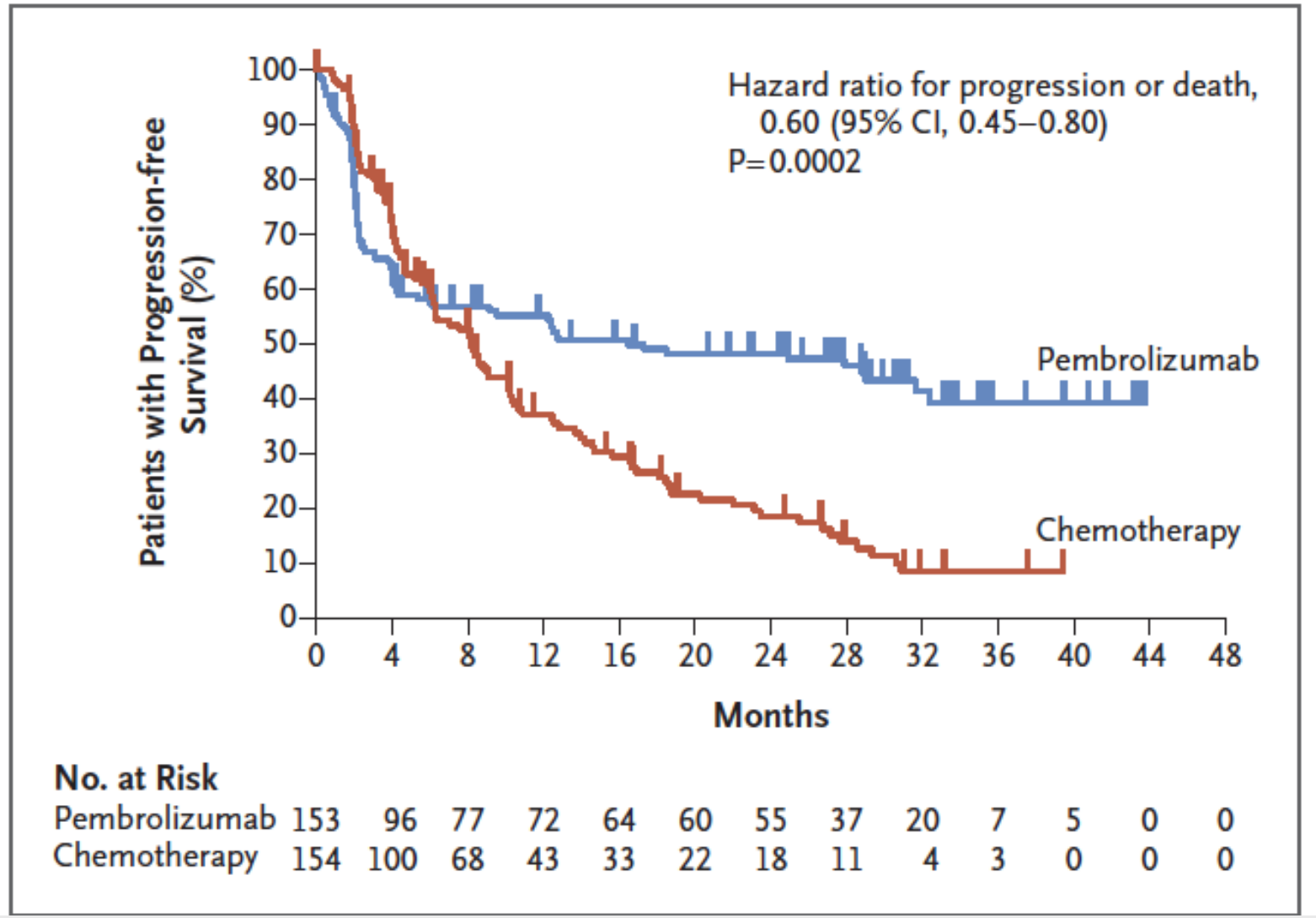
Collisson et al, Nat Can Rev 2019

Approved IO Targets



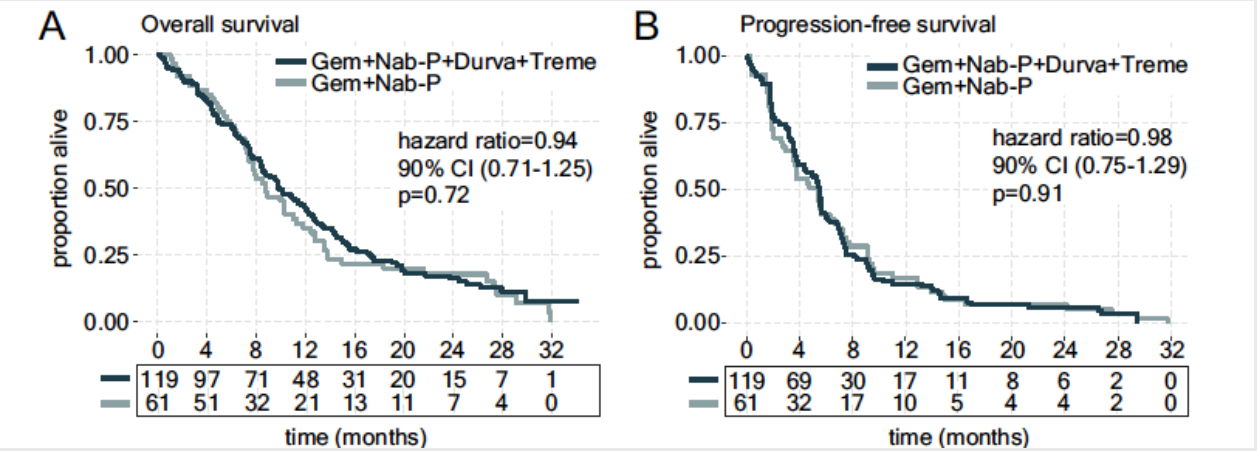
Ganesh et al, Nat Rev Gastroenterol Hepatol 2019

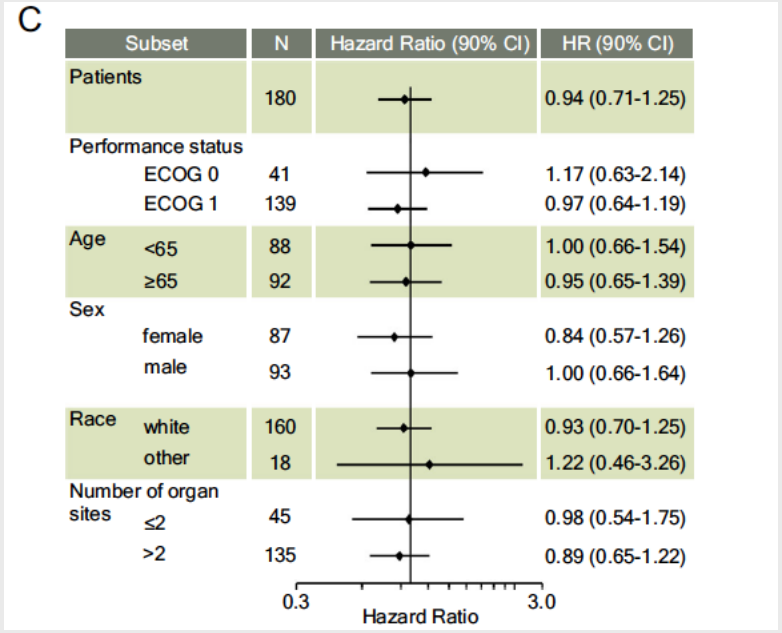
Pembrolizumab in MSI CRC

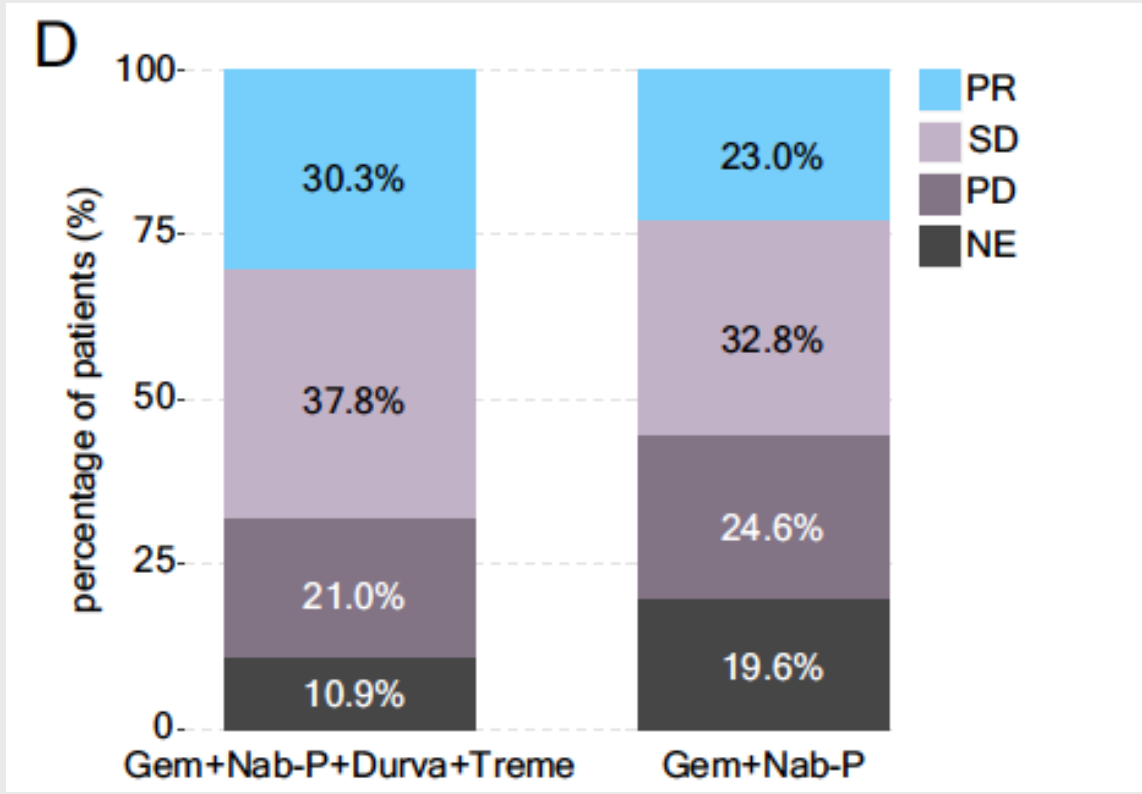


Andre et al, NEJM 2020

Current IO in PDAC

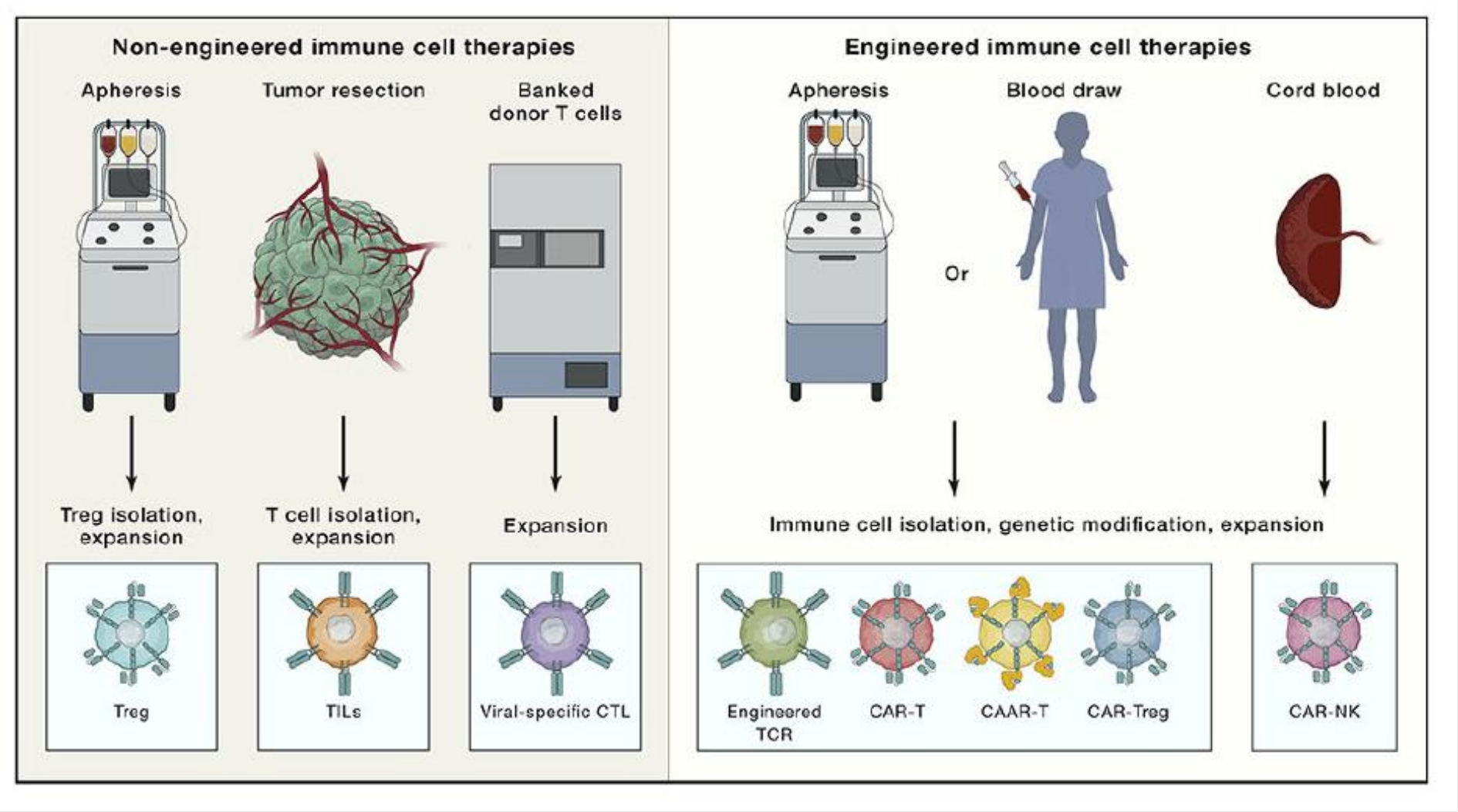






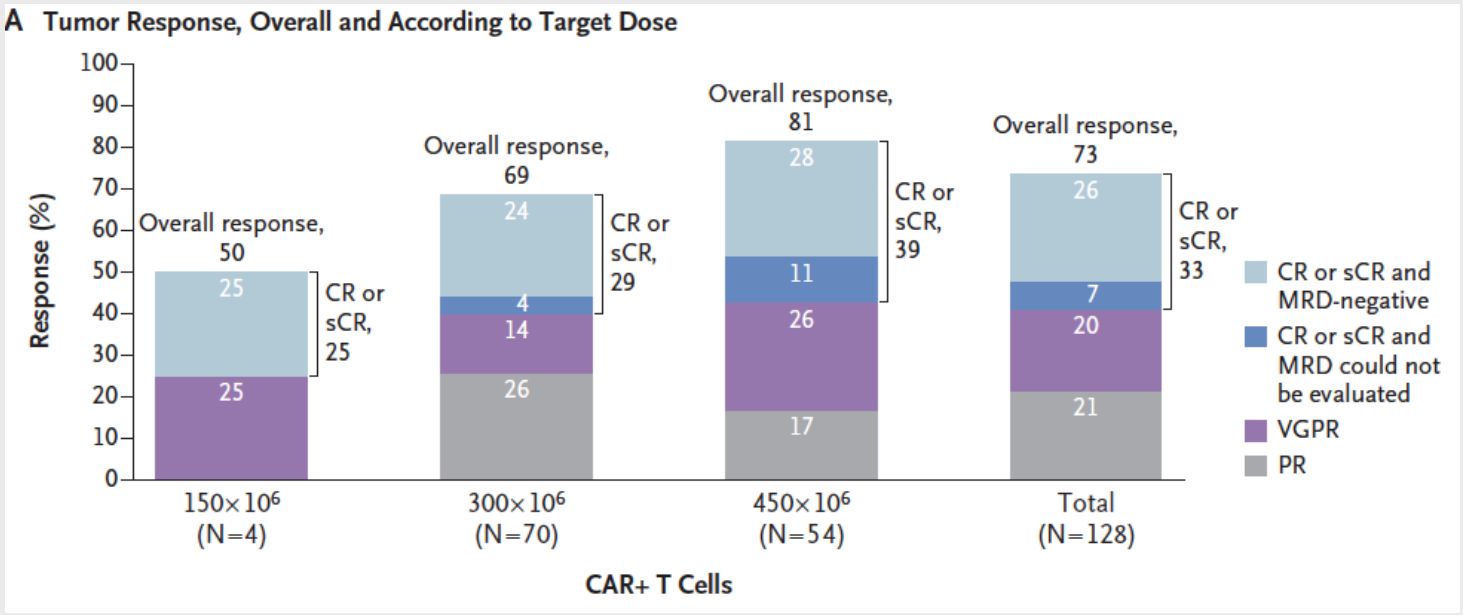
Renouf at al, Nat Com 2022

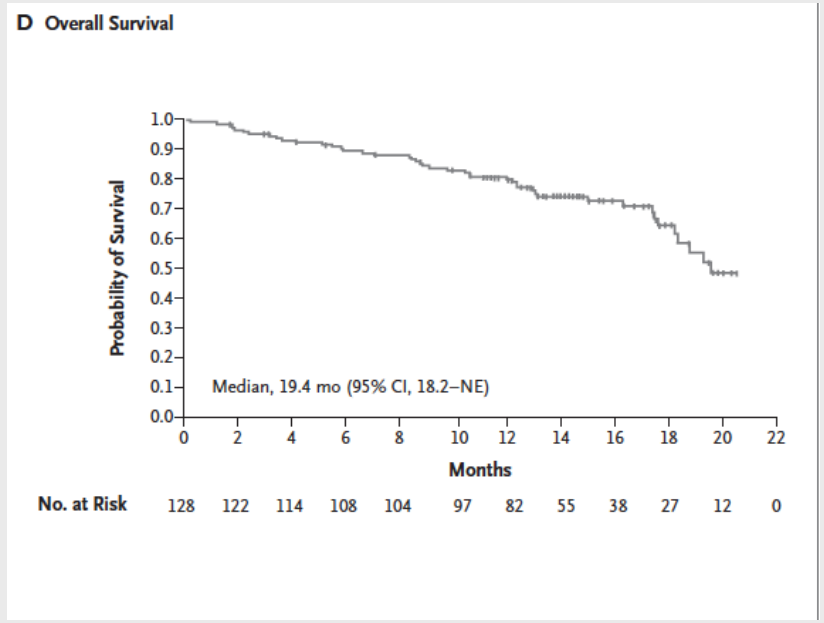
The Continuum of Immune Cell Therapies



Weber at al, Cell 2020

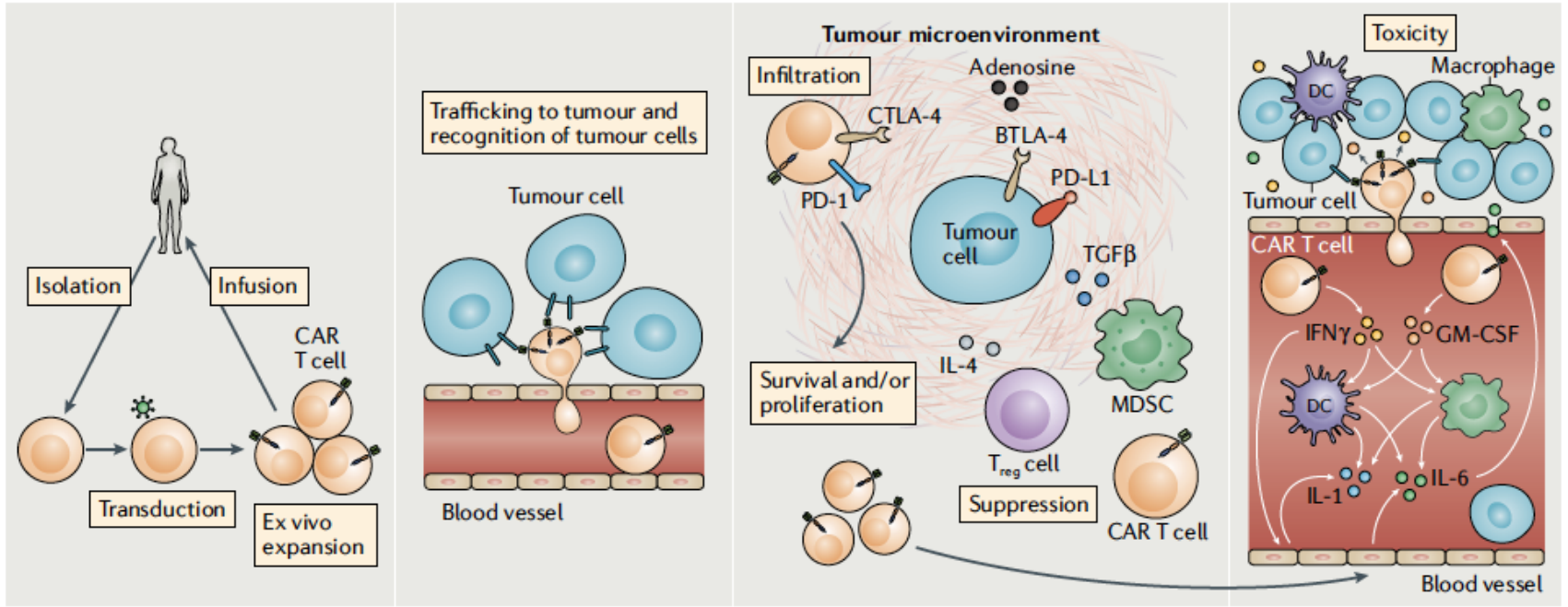
Ide-cel in RR Multiple Myeloma





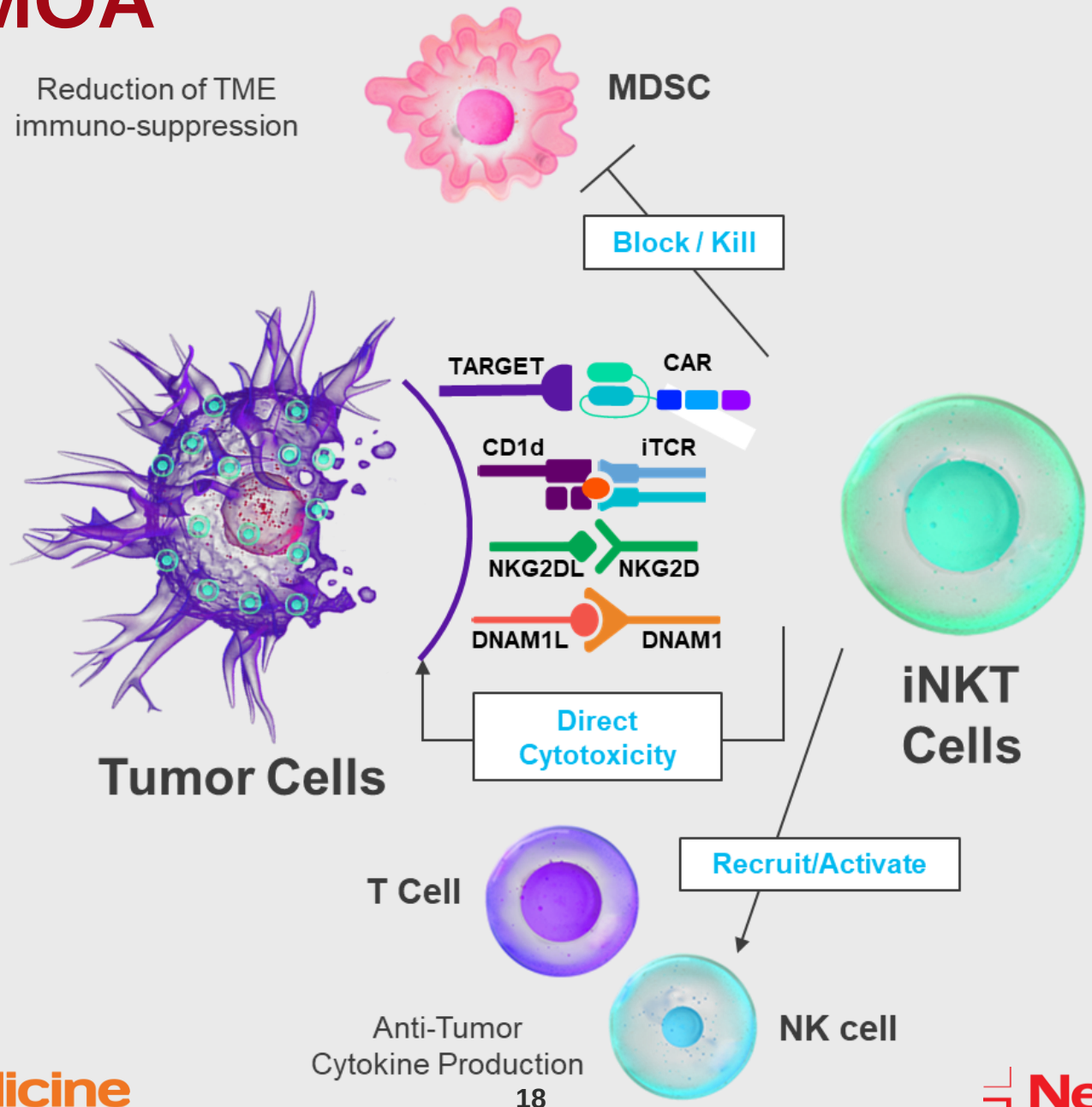
Munshi et al, NEJM 2021

Challenges with CAR T cells



Obstacles			
• Lymphopenia • T cell phenotype • Inherent T cell defects • Manufacturing time	• Homing to tumour tissues • Tumour cell heterogeneity for antigen expression	• Physical barriers • Inhibitory ligands • Immunosuppressive cells (T_{reg} cells and MDSCs) • Antigen escape • Excessive co-stimulation	• On-target, off-tumour toxicities • CRS • ICANS
Engineering solutions			
• Allogeneic donor T cells • Off-the-shelf CAR T cells	• Chemokines • Multispecific CARs • BiTEs	• Alter CAR structure • Cytokines • Ligands • Enzymes • BiTEs • scFv • Switch and/or dominant-negative receptors	• Alter CAR structure • Co-expression of factors • Safety switches • Logic gating and/or small-molecule adapters

iNKT cells MOA



Today we will hear…

- Allogeneic unmodified iNKTs (agenT-797) show reductions in target and non-target lesions or disease stabilization in patients with solid tumor cancers when administered alone [27%] and in combination with pembrolizumab (KEYTRUDA®) or nivolumab (OPDIVO®) [66%].

- agenT-797 shows 70% survival in severe viral ARDS compared to reference controls (~10%); potential for a variant agnostic approach to severe infections and pulmonary diseases.

- MiNK's FAP-CAR-iNKT, MiNK-215, demonstrates robust efficacy in NSCLC models, promoting curative responses, eliminating tumor burden in the lungs, and enhancing tumor specific CD8+ T cell infiltration through tumor stroma.

- MiNK-413 is a differentiated allogeneic IL-15-armored-BCMA-CAR-iNKT, a next generation approach to overcome the limitations of current autologous cell therapies.

- Allo-iNKTs (agenT-797) reinvigorates partially exhausted T cells and improves effector functions within the tumor microenvironment; critical mechanisms in rescuing PD-1 refractory tumors.

Dr. Mark Exley, PhD

Scientific Advisory Board Member, MiNK

- Expert in INKT biology and therapeutics in cancers, infections, auto-immunity and inflammation.
- Associate Editor of Clinical Immunology and >120 peer-reviewed publicatoins
- Faculty at Harvard Medical School
- Co-founder of NKT Therapeutics Inc.
- Professor at University of Manchester, UK.

MANCHESTER 1824
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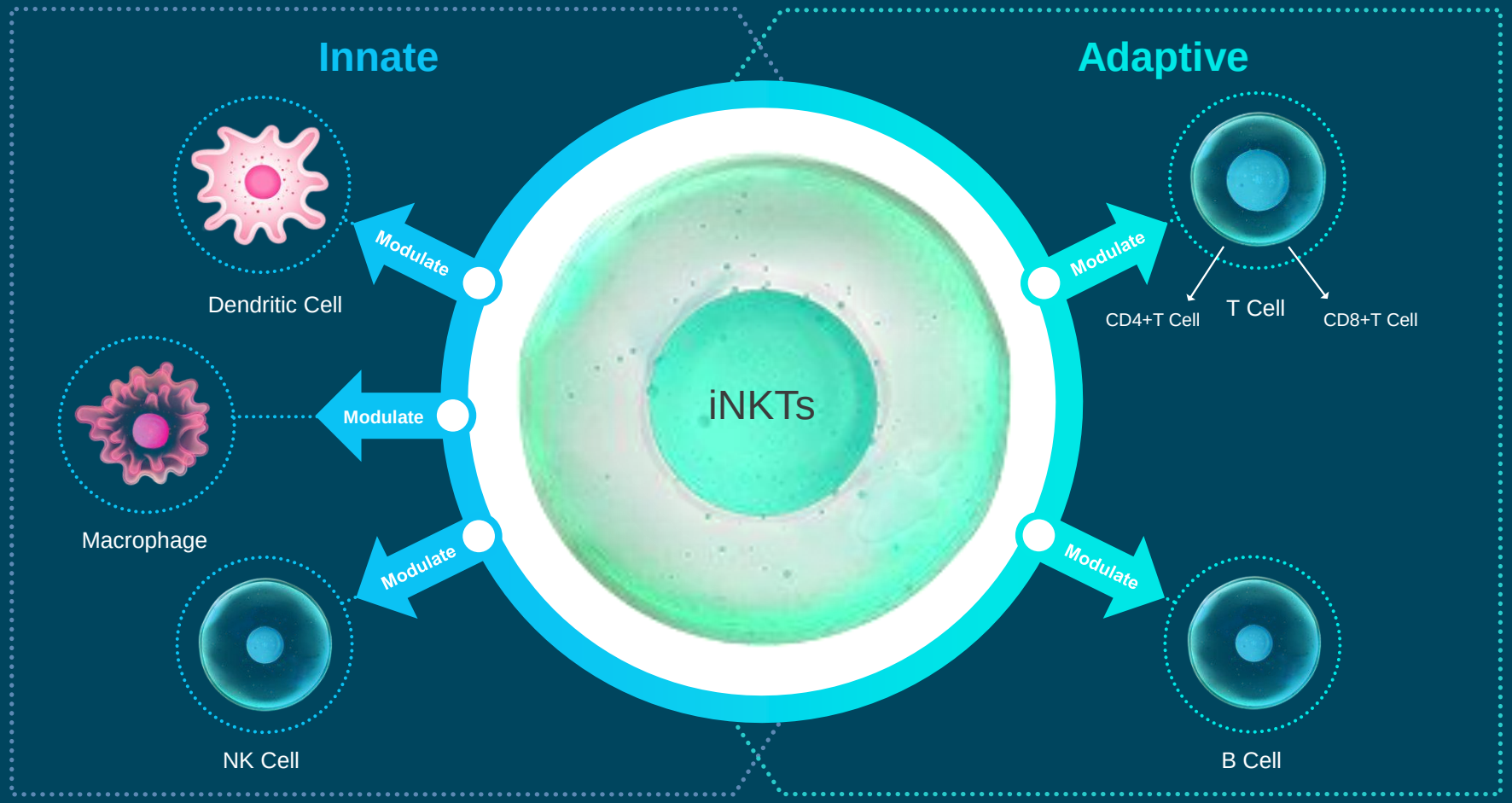
iNKT Cells are Distinct in the Cell Therapy Landscape, Combining both Innate and Adaptive Immunity



Rapid Response

Distinct T cells that possess the **effector function** of adaptive immune cells, but also the **rapid activation** kinetics of innate immune cells

Potent Activity

While rare in circulation, iNKTs can **amplify & accelerate** immune surveillance and response

Flexible Platform

Polarization of iNKTs towards pro- or anti-inflammatory states can tailor activity for specific indications

The University of Manchester

iNKT Cells Directly Attack Tumor Cells, Recruit Host Immunity, and Reshape Tumor Microenvironment

iNKT Anti-Cancer Mechanism

Direct tumor killing

Granzyme B secretion upon 2 iNKT-tumor interactions:

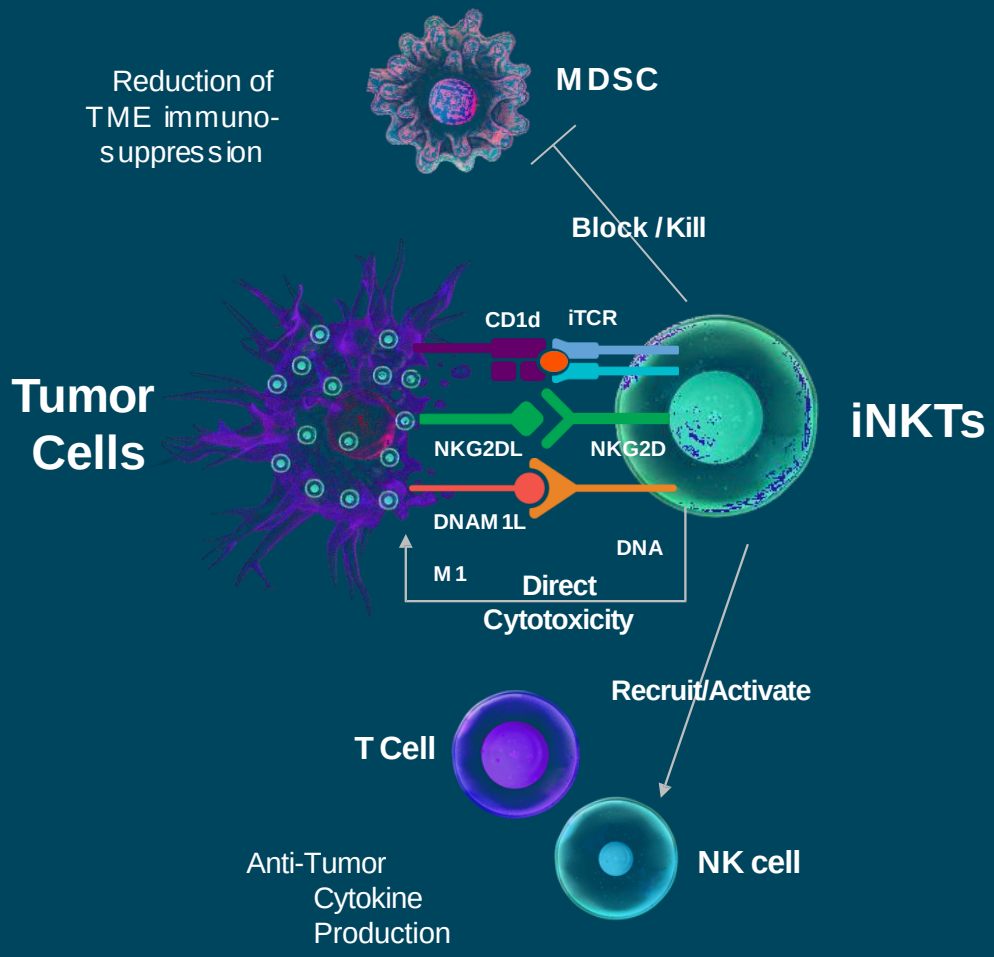
- Invariant TCR binding to glycolipids presented by CD1d
- NKG2D and DNAM-1 detection of tumor cell ligands

Recruitment of host immunity

- Recruitment of host T cells and NK cells
- Restoring the cytotoxic capacity, activation, and cytokine production of partially exhausted T cells

Conditioning of tumor microenvironment

- Activating dendritic cells for enhanced antigen presentation
- Preferentially killing tumor-promoting M2 macrophages while preserving pro-inflammatory M1 macrophages



Adapted from: Wolf, B., Exley, M. et al. Frontiers in Immunology. 2018

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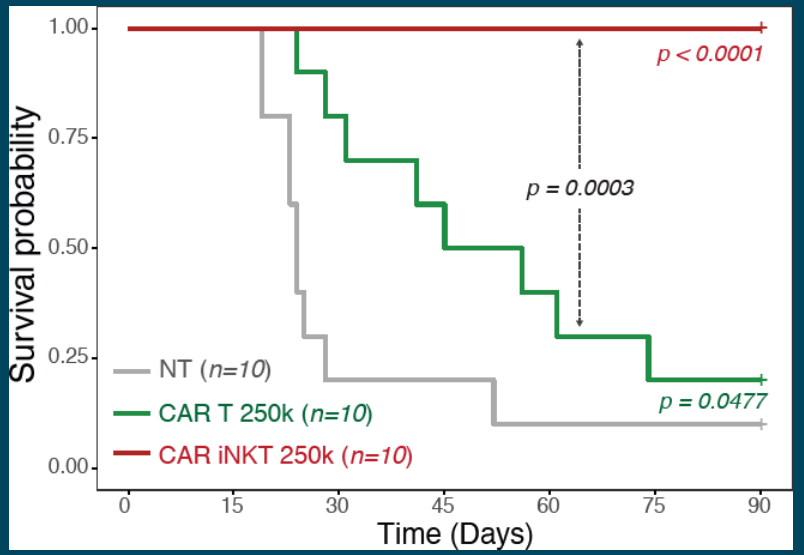
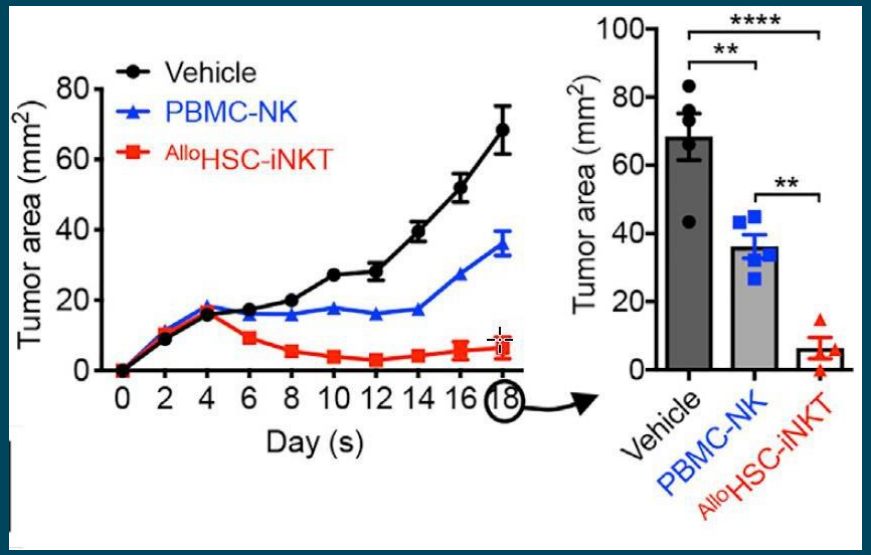
iNKTs Promote Superior Tumor Control and Survival Relative to T and NK Cells

CAR-iNKT Promote Superior Survival vs CAR-Ts Through Direct Killing & Host Immunity Induction



- CD19-CAR-iNKTs promoted superior tumor control relative to CAR-T cells, resulting in **survival of all mice**
- CAR-iNKTs uniquely **induce host CD8 T-cell responses**, resulting in a potent antitumor effect lasting **longer than the persistence of allogeneic cells**

iNKT Outperform NK Cells Through Intrinsic NK Function



- iNKT cells more effectively **suppress tumor growth** than NK cells
- iNKTs promote superior antitumor responses through increased expression of **NK activating receptors**, reduction of **NK inhibiting receptors** and **production of cytotoxic molecules**

Adapted from: Simonetta, J et al. Clin Cancer Res. 2021, Li, Y et al. Cell Reports Medicine. 2021

iNKTs in ARDS and Viral Infections

iNKT Anti-Infection Mechanism

Direct viral killing

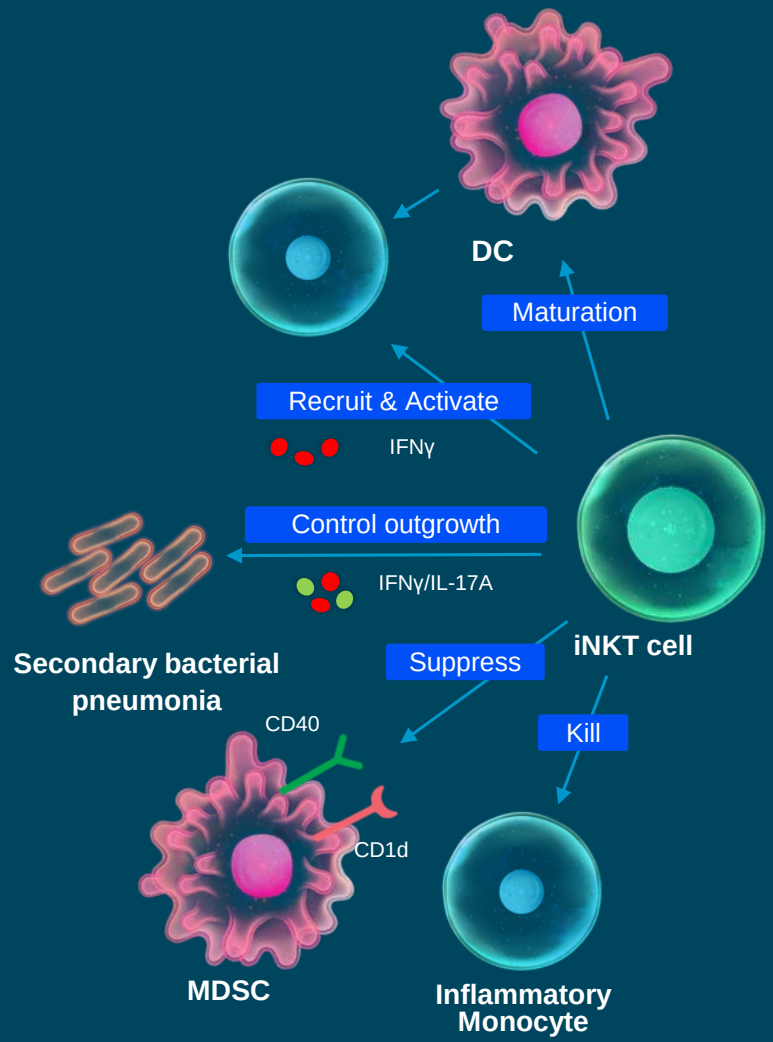
- Recognition of CD1d ligands in diseased tissue and activation through the invariant TCR
- Recognition of stress-signals through activating NK receptors, NKG2D, DNAM1

Recruitment of host immunity

- Recruitment of host T cells and NK cells
- Restoring the cytotoxic capacity, activation, and cytokine production of partially exhausted T cells

Conditioning of infection site

- Kills inflammatory monocytes (protects airway epithelium)
- Induces maturation of immature DCs
- Dampens pro-inflammatory cytokines (i.e. IL-1, IL-6)



Adapted from: Wolf, B et al. Frontiers in Immunology. 2018

24

iNKT Cells Have Benefits Beyond Other Cell Therapies

		iNKT Cells	T Cells	NK Cells	γδ T Cells
POTENT CANCER KILLING	**Tumor homing** and persistence	✓	✗	✗	✓
	Orchestrate **innate** and **adaptive** immune responses	✓	✗	✗	✗
	Modulate suppressive **myeloid** compartment	✓	✗	✗	✗
ENHANCED TOLERABILITY	**No TCR engineering** needed for allogeneic application	✓	✗	✓	✓
	No lymphodepletion; naturally **suppresses GvHD**	✓	✗	✗	✗
	Ability to **multi-dose** and administer **without lymphodepletion**	✓	✗	?	?
OFF-THE-SHELF APPROACH	Scalable, off-the-shelf proprietary process **scaling >10,000 doses/yr**	✓	?	?	?

25

The University of Manchester

Dr. David Einstein, MD

Lead Investigator

- Genitourinary Medical Oncologist, Beth Israel Deaconess Medical Center
- Assistant Professor, Harvard Medical School
- Director, GU Oncology Clinical Research, Beth Israel-Lahey Network
- Principal Investigator of the DF/HCC GU Rapid Autopsy Program
- Young Investigator and Challenge Awards from the Prostate Cancer Foundation for investigation of immunogenic prostate cancer
- Principal Investigator or Co-Investigator on multiple DF/HCC clinical trials of immune-based and targeted therapies for GU cancers

Beth Israel Lahey Health

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Allo-INKTs (agent-797) Alone or In Combination with PD-1 Inhibitors Builds on Observations of Activity of iNKTs in Solid Tumors

Autologous INKTs in Solid Tumors	Clinical Outcomes
Head and Neck Cancer (SCCHN)	ORR: 50%
Non-Small Cell Lung Cancer (NSCLC)	SD: 67% (4/6)
Advanced Hepatocellular Carcinoma (HCC)	mOS: 13 months Historical: <6 months

Favorable safety with four Grade 3 AEs (n=43 patients in 5 trials); no serious cytokine release or neurotoxicity; up to 1 billion cells per patient, comparable to approved cell therapies[1]

Adapted from: Yamasaki et al, Clin Immunol 2011; Exley et al, Clin Cancer Res, 2017; Gao et al, Oncologist 2021

iNKT Cells Plus Checkpoint Inhibitors Show Solid Tumor Elimination

Syngeneic Checkpoint Inhibitor-Resistant Melanoma Tumor Model (B16-Ova)

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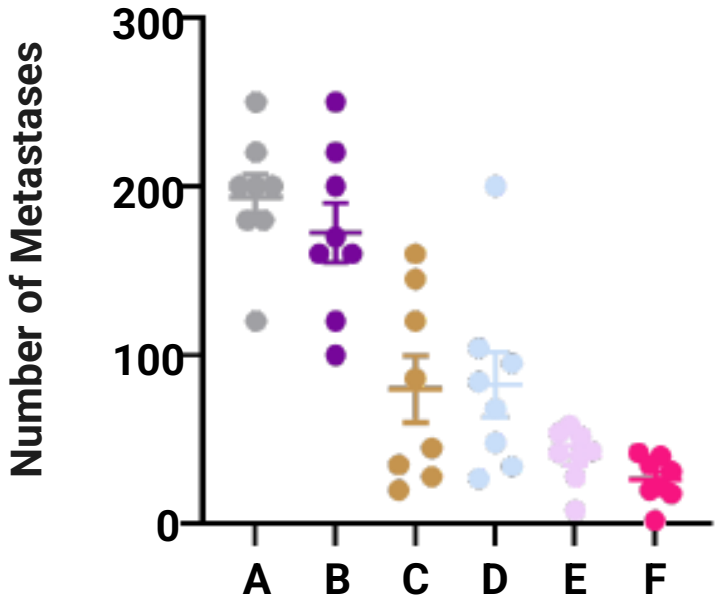

A Control
B Fc enhanced CTLA-4 + PD-1
C iNKT activator
D iNKT activator + PD-1
E iNKT activator + Fc enhanced CTLA-4
F iNKT activator + Fc enhanced CTLA-4 + PD-1

- Endogenous iNKTs activated by administration of α-GalCer
- Activated iNKTs show effective tumor infiltration and reduction
- **Combination of activated iNKTs with PD-1 and CTLA-4 checkpoint antibodies show clearance of lung metastases**

Source: Tanne et al. AACR 2020, Poster 922

B16ova melanoma model resulting in lung metastases after intravenous injections

Phase 1 Trial of agent-797 (allo-iNKTs) Monotherapy or in Combination with Pembrolizumab or Nivolumab in Solid Tumors

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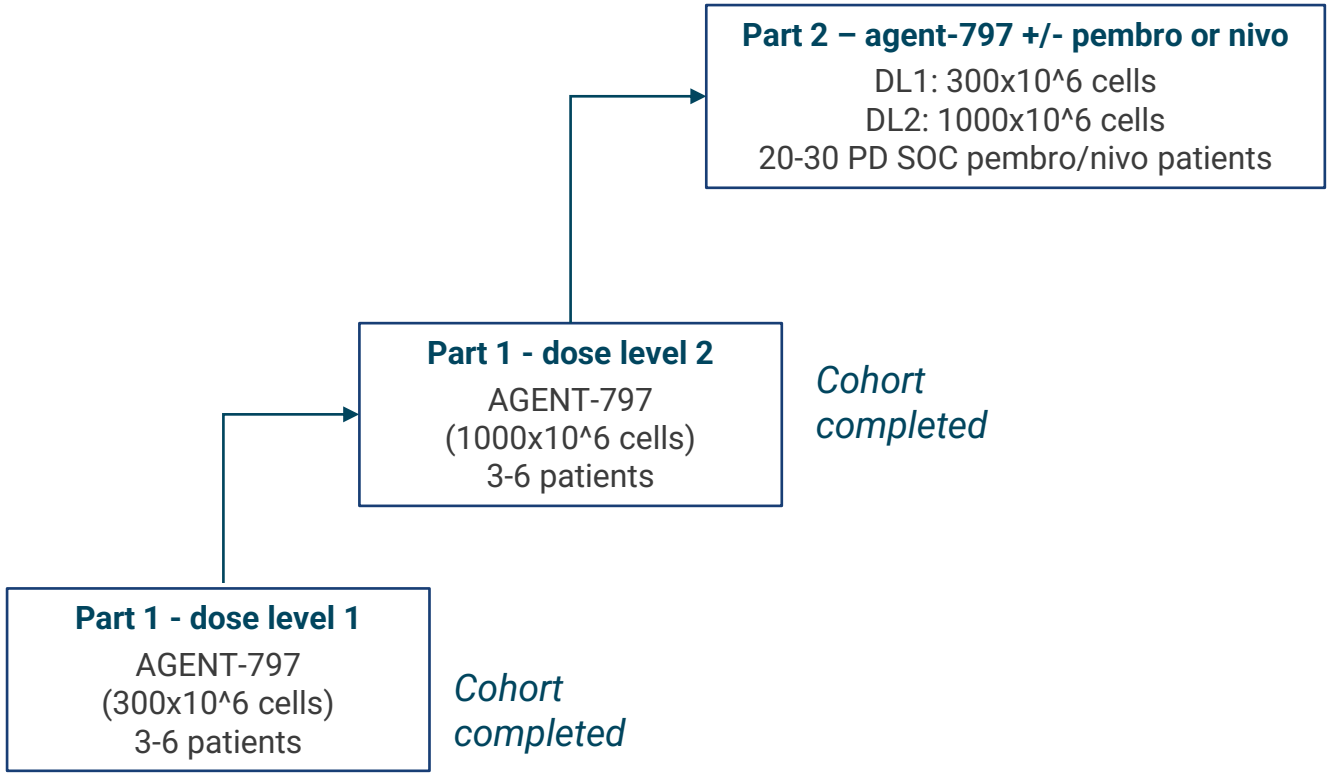

Primary endpoints

- Dose relationship and AEs
- Safety, PD, PK, DLTs and RP2D

Secondary endpoints

- Persistence of AGENT-797
- Clinical response: ORR, DOR, PFS, and TTR
- Alloantibodies to MHC I/II and impact of HLA mismatch

Exploratory endpoints

- agenT-797 phenotypic and functional alterations in blood and tissue
- agenT-797 impact on immune profile, immune activation, anti-tumor immunogenicity, gene expression in tumor and TME
- Impact of HLA mismatch on iNKT persistence and activity

Expansions at RP2D in solid tumor cancers, including but not limited to NSCLC, HCC, prostate

Source: Stevens et al, SITC 2022, Poster 649

Phase 1 Trial of agent-797 (allo-iNKTs) Monotherapy or in Combination with Pembrolizumab or Nivolumab in Solid Tumors

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Phase 1 Overview

	DL1 $4.3x10^6$ cells/kg N=8	DL1 4.3×10^6 cells/kg + pembro/nivo N=3	DL2 1.4×10^7 cells/kg N=14	Total N=25
Age				
Median (range)	60 (30-73)	62 (62-76)	57 (54-66)	62 (30-76)
Sex, n (%)				
Male	2 (25.0)	3 (100.0)	11 (78.6)	16 (64.0)
Female	6 (75.0)	0	3 (21.4)	9 (36.0)
Patient Disposition				
Early d/c	6 (75.0)	1 (33.3)	2 (14.3)	9 (36.0)
Death	1 (12.5)	0	0	1 (4.0)
Progression	5 (62.5)	1 (33.3)	2 (14.3)	8 (32.0)

- **Trial Launch May 2022**
- Efficacy Evaluable/Enrolled: 14/25
- Heavily pretreated with median ~4 prior lines of therapy
- Median follow-up ~18 weeks
- Favorable safety; no CRS or neurotoxicity

agenT-797 Shows Early Signs of Clinical Activity in Solid Tumors

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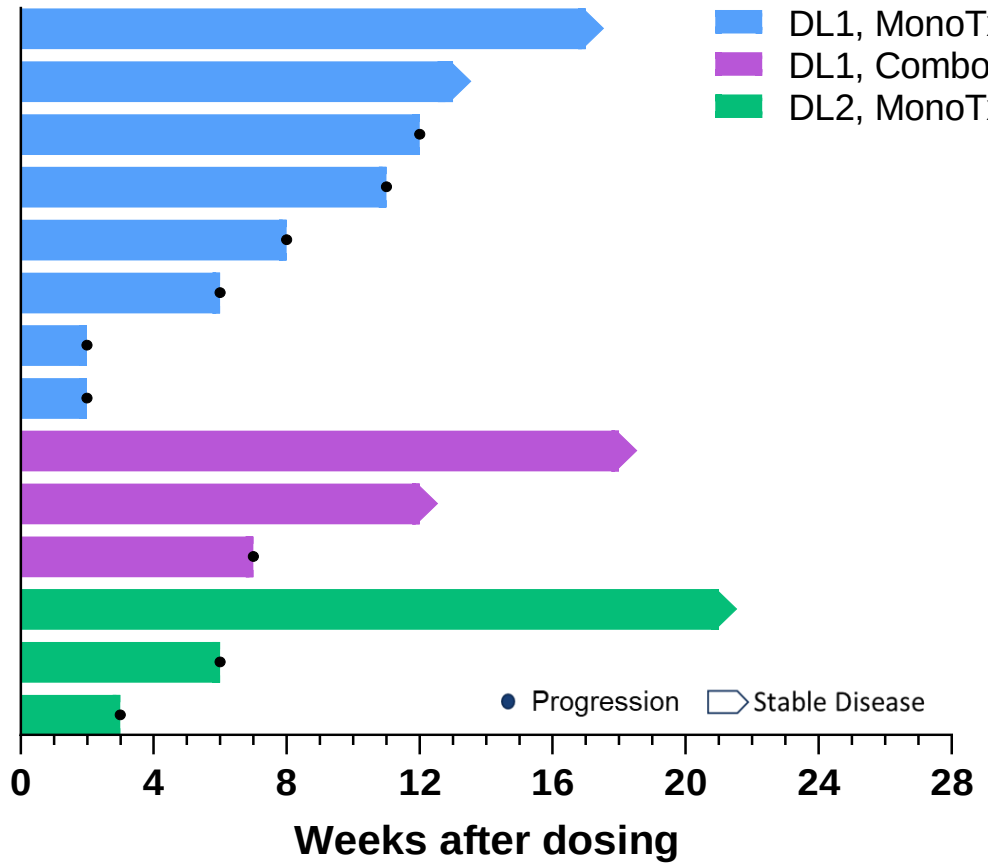
Reduction in Target and Non-Target Lesions in Heavily Pre-treated Patients



Preliminary Activity in Heavily Pre-treated Patients

- Reduction of target and non-target lesions or disease stabilization in patients treated with agenT-797 alone (27%) or in combination with pembro/nivo (66%)
- Disease stabilization observed after failure of SOC and progression on checkpoint inhibitors

Cancer	Dose Level (cells)	# Prior Lines	Response (weeks)
Pancreatic	**300 x 10^6 (mono)**	**3**	**Stable Disease 18+**
Thymoma	**300 x 10^6 (mono)**	**4**	**Stable Disease 14+**
NSCLC	**300 x 10^6 (combo)**	**6**	**Stable Disease 19+**
Gastric	**1000 x 10^6 (combo)**	**2**	**Stable Disease 12+**
Appendiceal	**1000 x 10^6 (mono)**	**3**	**Stable Disease 22+**

agenT-797 Can Be Dosed Alone and In Combo with Anti-PD-1 with Favorable Tolerability Profile

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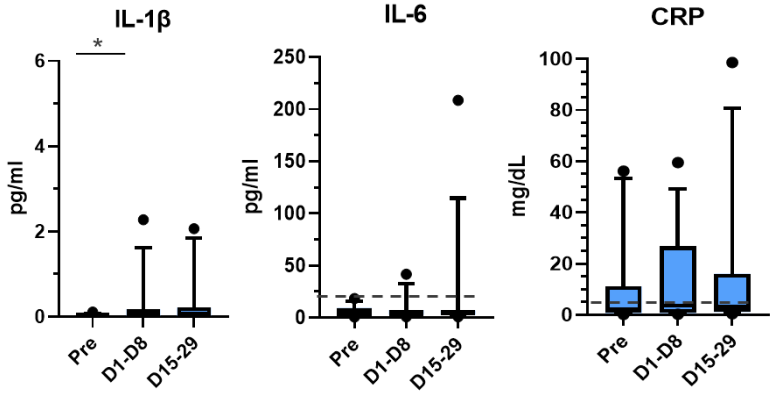
No DLTs and Few Related AEs

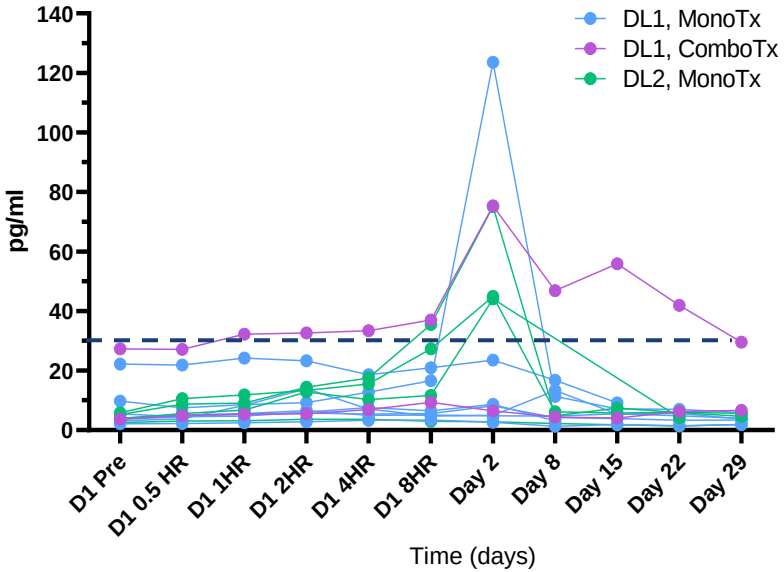
Summary of Related Adverse Events	Solid Tumors (n=25)
Any AE grade ≥ 3	8 (32%)
Any TRAE grade ≥ 3	1 (4%)
Any irAE	0 (0%)
Any TRAE leading to discontinuation	0 (0%)
Any TRAE leading to dose interruption	0 (0%)
Any TRAE leading to death	0 (0%)

- Solid tumors: one TRAE of grade ≥3 (anemia)
- Multiple myeloma: TEAEs of grade ≥3 were observed in 2 subjects (thrombocytopenia)
- Most common TEAEs were fatigue, nausea, constipation, dizziness, anemia

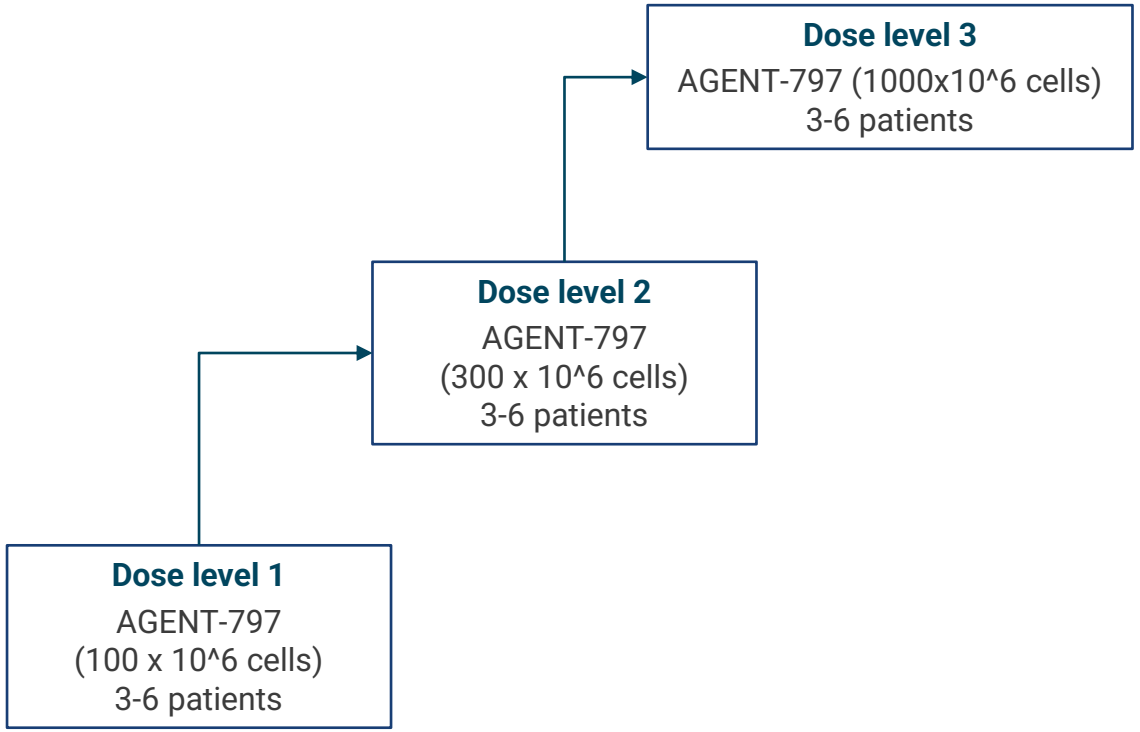
No Cytokine Release Syndrome or Neurotoxicity



agenT-797 Shows Modulation of IFNɣ



Phase 1 Trial of agenT-797 in R/R Multiple Myeloma After ≥3 Prior Lines of Therapy



Enrollment completed in all dose levels

Primary endpoints

- Dose relationship and AEs
- Safety, PD, PK, DLTs and MTD

Secondary endpoints

- Persistence of AGENT-797
- Clinical response: ORR, DOR, PFS, and TTR
- Alloantibodies to MHC I/II and impact of HLA mismatch

Exploratory endpoints

- agenT-797 phenotypic/functional alterations
- agenT-797 impact on immune profile, immune activation, anti-tumor immunogenicity, gene expression and TME
- Impact of HLA mismatch on iNKT persistence and activity

Source: Stevens et al, SITC 2022, Poster 649

agenT-797 Shows Early Clinical and Biomarker Activity in r/r Multiple Myeloma After ≥3 Prior Lines of Therapy

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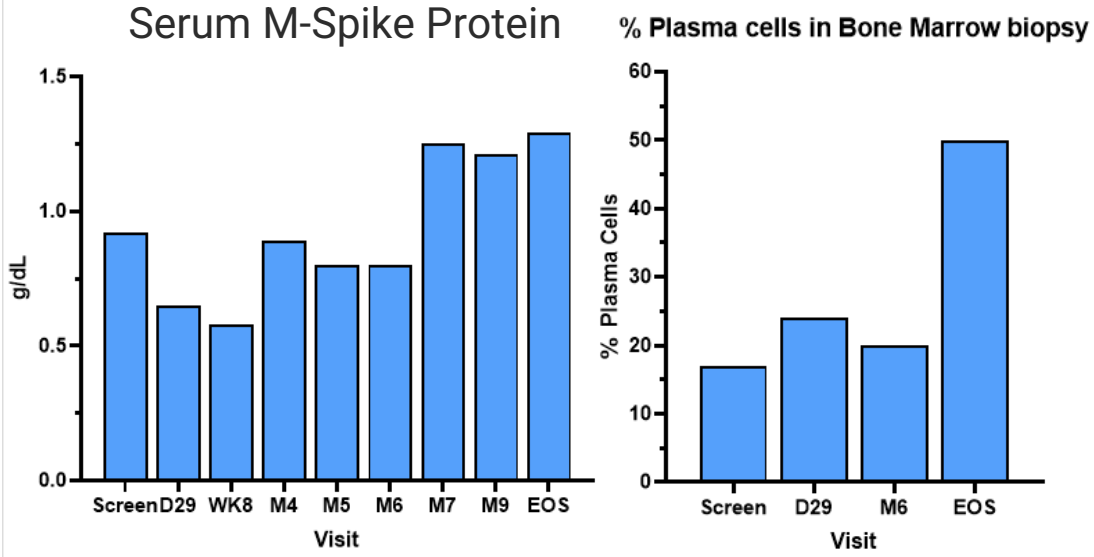
Durable disease stabilization for over 10 months in heavily pre-treated patients

Patient	Dose Level (cells)	# Prior Lines	Response (months)
1	**100 x 10^6**	**6**	**SD10**
2	100 x 10^6	6	PD
3	100 x 10^6	4	PD
4	300 x 10^6	4	PD
5	300 x 10^6	3	PD
6	**300 x 10^6**	**7**	**SD2+**
7	1000 x 10^6	2	PD
8	1000 x 10^6	6	PD

Case Study: Reduction in M-spike protein and stabilization of plasma cell levels



Source: Stevens et al, SITC 2022, Poster 649

agenT-797 Administered Without Lymphodepletion in MM with a Favorable Safety Profile

Beth Israel Deaconess Medical Center

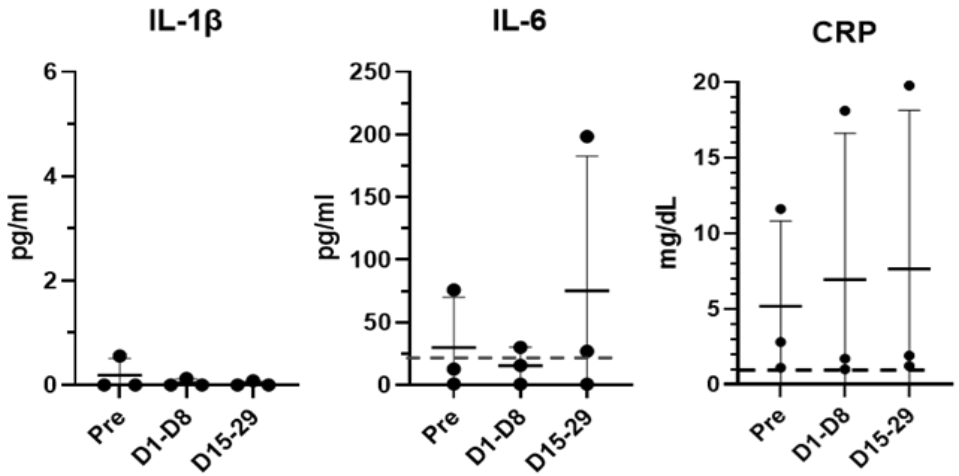
HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

No DLTs and Few Related AEs

	Multiple Myeloma (n=12)
Any AE grade ≥ 3	2 (16.7%)
Any TRAE grade ≥ 3	0 (0%)
Any irAE	NR
Any TRAE leading to discontinuation	0 (0%)
Any TRAE leading to dose interruption	0 (0%)
Any TRAE leading to death	0 (0%)

- Solid tumors: one TRAE of grade ≥3 (anemia)
- Multiple myeloma: TEAEs of grade ≥3 were observed in 2 subjects (thrombocytopenia)
- Most common TEAEs were fatigue, nausea, constipation, dizziness, anemia

No Cytokine Release Syndrome or Neurotoxicity



Summary and Future Directions

- agenT-797 alone and in combination with anti-PD-1 is well tolerated across multiple doses and shows early signals of clinical and biomarker activity in patients with solid tumors and multiple myeloma
- No evidence of cytokine release, neurotoxicity, or immune related adverse events
- Observations may be related to INKT conversion of partially exhausted CD8+ T cells **(SITC #372)**, or effector functions within the tumor microenvironment (**SITC #372**)
- agenT-797 expansion trials in cohorts designed to expand benefit beyond available SOC, including, but not limited to lung and liver cancers are under development with agenT-797 alone and in combination with CPIs (anti-PD-1; **NCT05108623**)
- Considerations for future trial development
  - Triplet therapies based on tolerability and pre-clinical justification for combination with Agenus pipeline CPIs
  - Tolerability also supports moving into earlier disease spaces with potentially less immunosuppressive tumor immune microenvironments

Sapana Pokharel, PhD

Therapeutics Scientist
MiNK Therapeutics

MiNK Therapeutics

R&D DAY

Abstract Number: 372

agenT-797, a native allogeneic “off-the-shelf” invariant natural killer T (iNKT) cell therapy product improves effector functions within the tumor microenvironment

Novel therapeutic approaches therapies are required for redirecting dysfunctional T cells and myeloid cells for anti-tumor functions

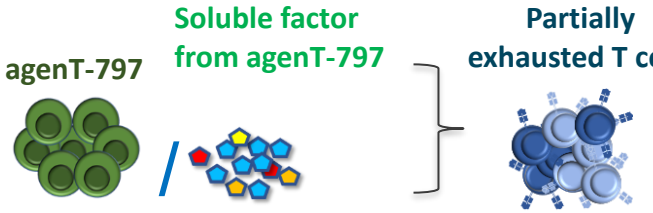
- T cell exhaustion is a common phenomenon that occurs due to prolonged antigen exposure during cancer and chronic viral infection. Despite the promising therapeutic effects of CAR-T therapy on hematological malignancies, limited effect on solid tumors and patients suffering from relapse is known with this therapy.

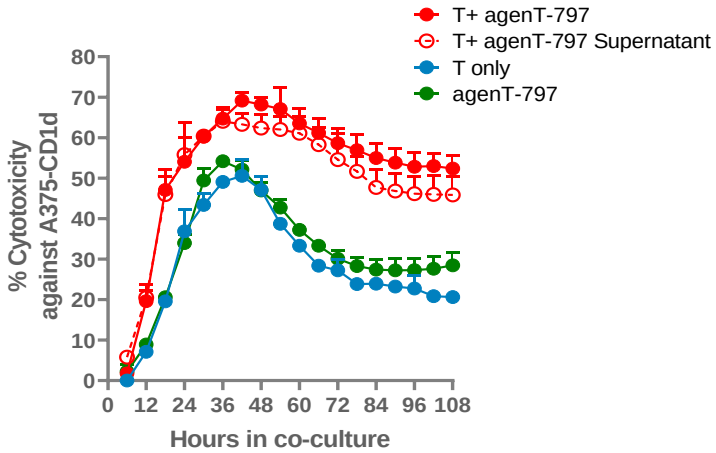
- Myeloid cells are most abundant immune cells in the tumor microenvironment which play a central role in mediating immunosuppression through direct contact or secretion of soluble factors.

- **agenT-797** is a native allogeneic “off-the-shelf” iNKT cell therapy product which is in clinical trial for heme malignancies, solid tumor and COVID . Here, we show that agenT-797 modulate the immune responses in tumor microenvironment by
    1. enhancing the killing potential of partially exhausted T cells
    2. activating the dendritic cells
    3. targeting immuno-suppressive macrophages

agenT-797 Improved Anti-Tumor Activity of Immune Cells that are Present in the Tumor Microenvironment

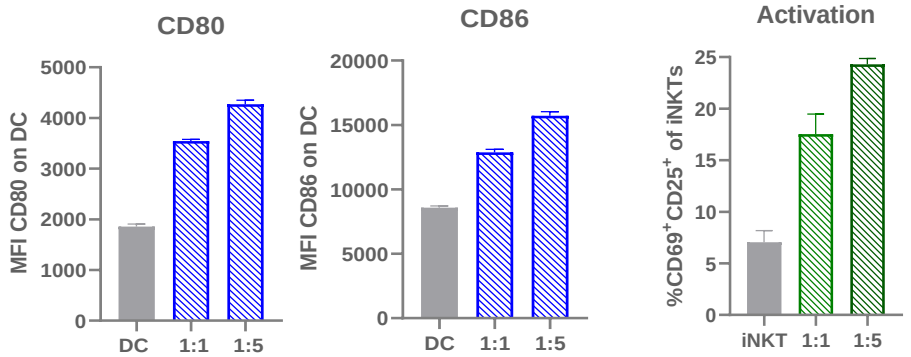
Enhanced Cytotoxic Response of partially Exhausted T cells





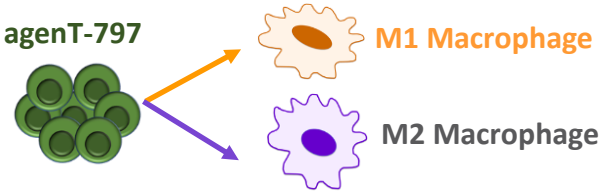
- agenT-797 enhances tumor killing by re-invigorating partially exhausted CD8⁺T cells via soluble factors

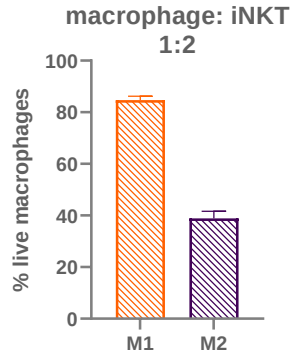
Promote trans-activation of Dendritic cells



- Activating dendritic cells which can promote activation of T cells through enhanced antigen presentation

Preferential killing of immuno-suppressive M2 macrophages





- agenT-797 selectively kills M2 macrophages while preserving M1 macrophages for anti-tumor responses

MiNK Therapeutics

MiNK Therapeutics

R&D DAY

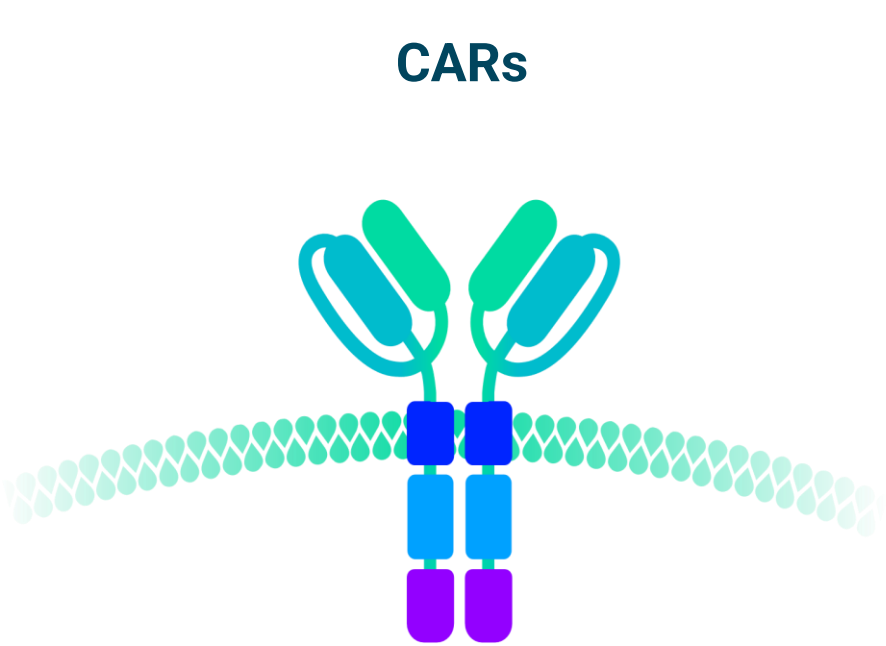
Optimizing iNKT Cells

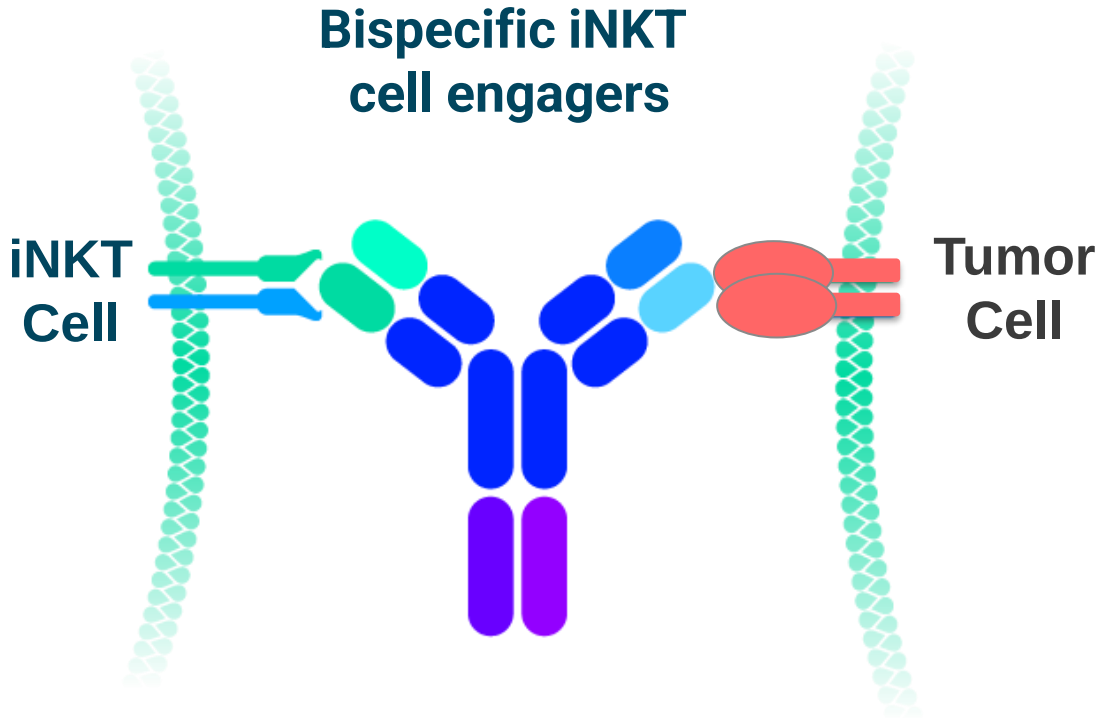
Our Platforms for CAR-INKT and INKT-Engagers

Marc van Dijk

Chief Scientific Officer
MiNK Therapeutics

iNKT Cell Anti-Tumor Activity Can be Enhanced by CARs and Engagers





CARDIS™ Platform
CARs to surface-expressed antigens

Bispecific iNKT Cell Engager Platform
IgG-based iNKT cell engagers

MiNK Therapeutics

iNKT Cell Anti-Tumor Activity Can be Enhanced by CARs and Engagers

iNKT Anti-Cancer Mechanism

Direct tumor killing

Granzyme B secretion upon 2 iNKT-tumor interactions:

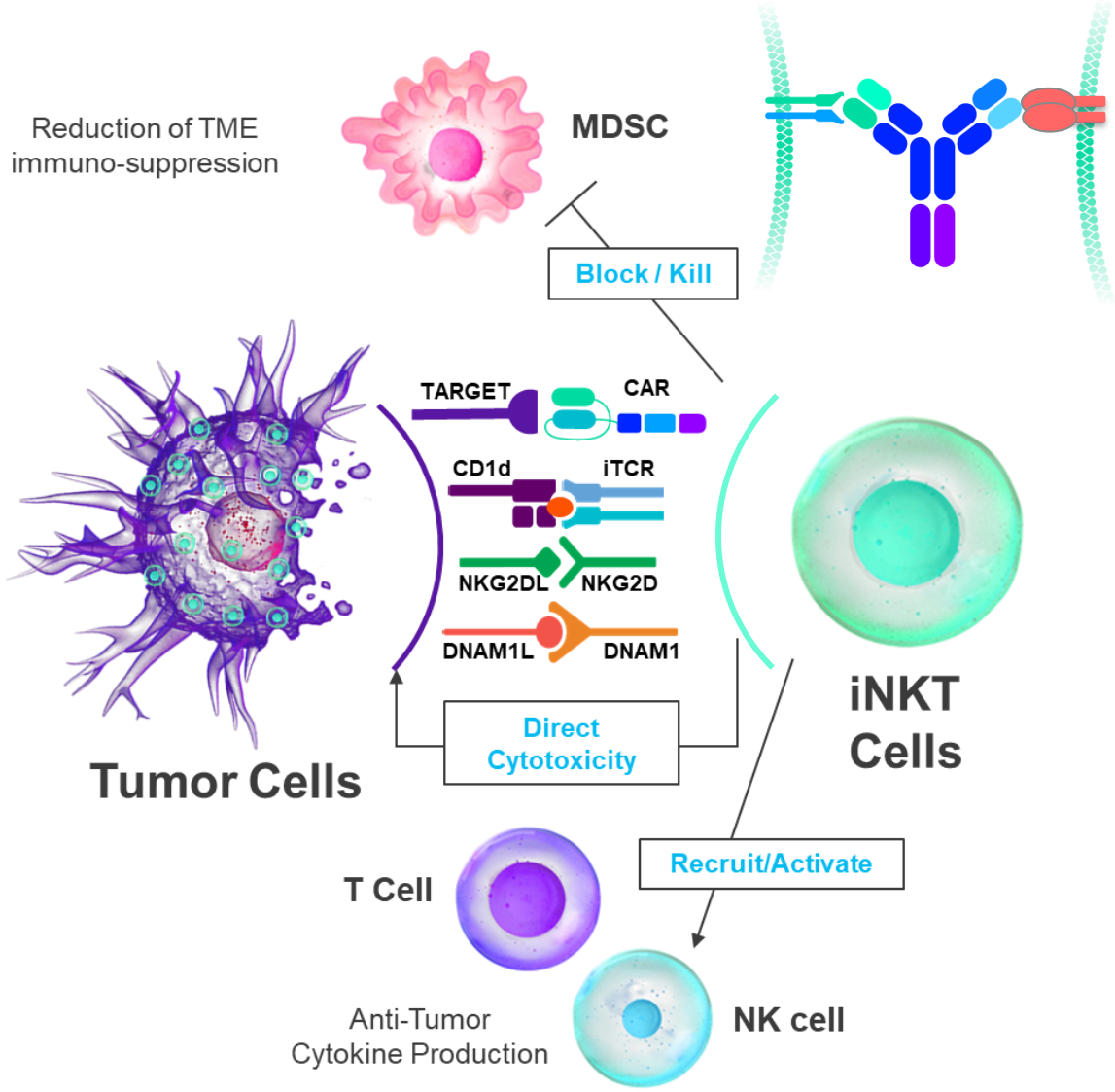
- Invariant TCR binding to glycolipids presented by CD1d
- NKG2D and DNAM-1 detection of tumor cell ligands

Recruitment of host immunity

- Recruitment of host T cells and NK cells
- Restoring the cytotoxic capacity, activation, and cytokine production of partially exhausted T cells

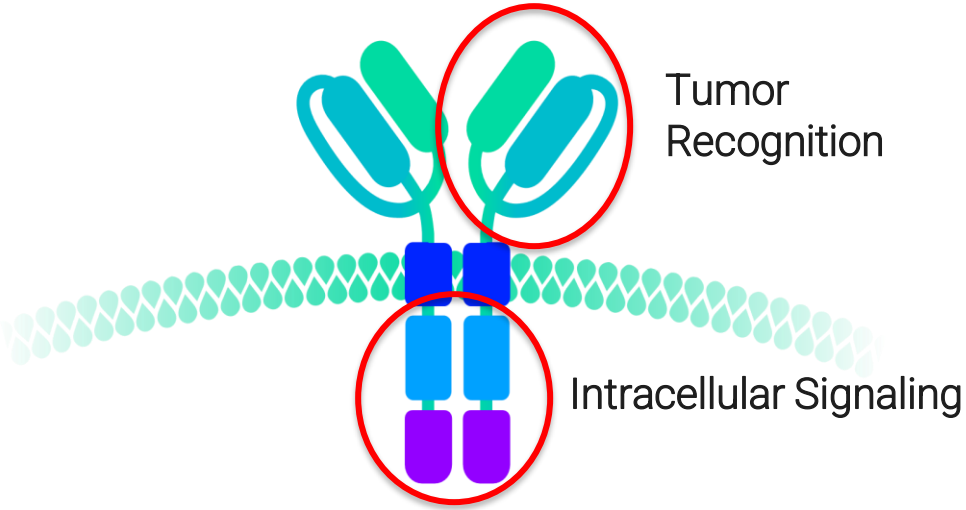
Conditioning of tumor microenvironment

- Activating dendritic cells for enhanced antigen presentation
- Preferentially killing tumor-promoting M2 macrophages while preserving pro-inflammatory M1 macrophages

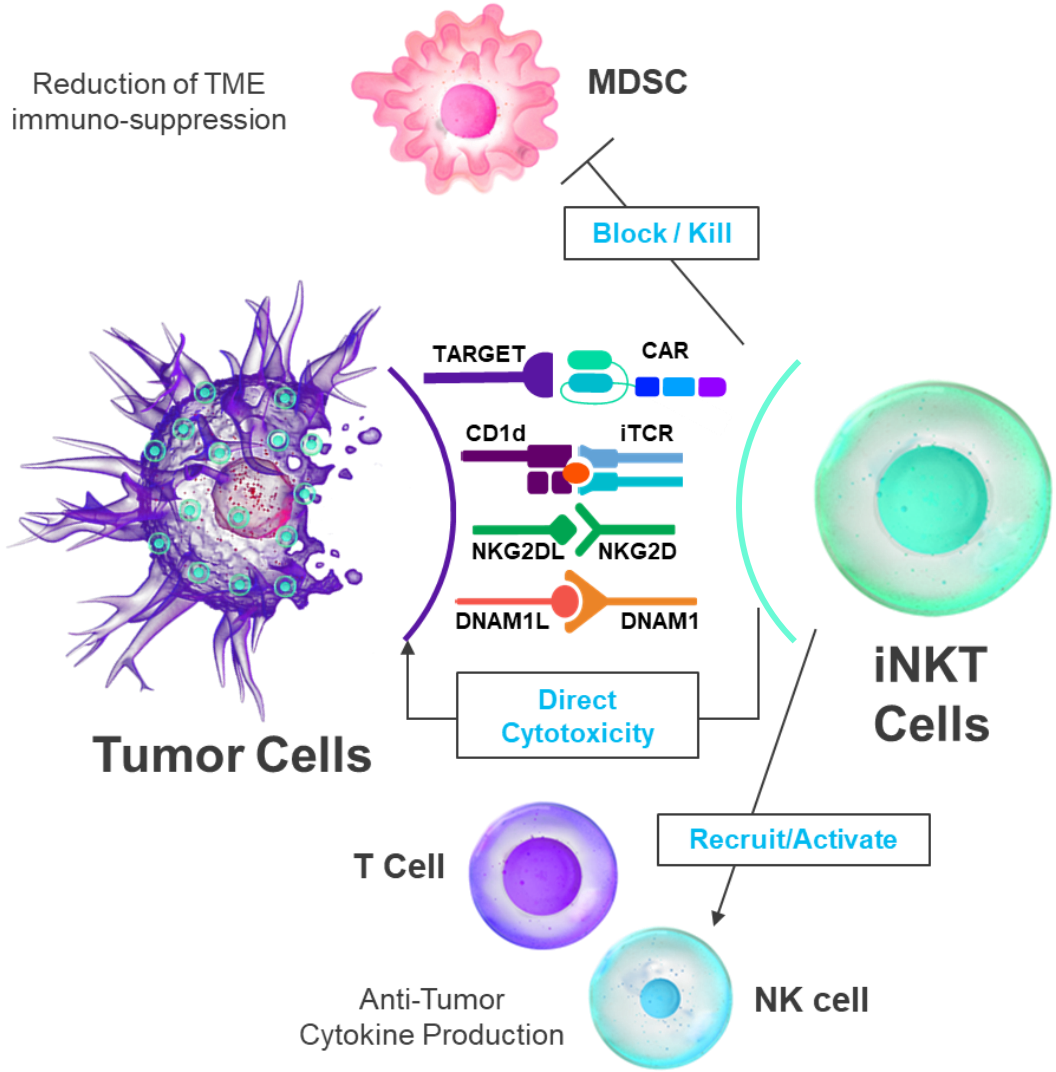


CARDIS Platform - Chimeric Antigen Receptors for iNKT cells

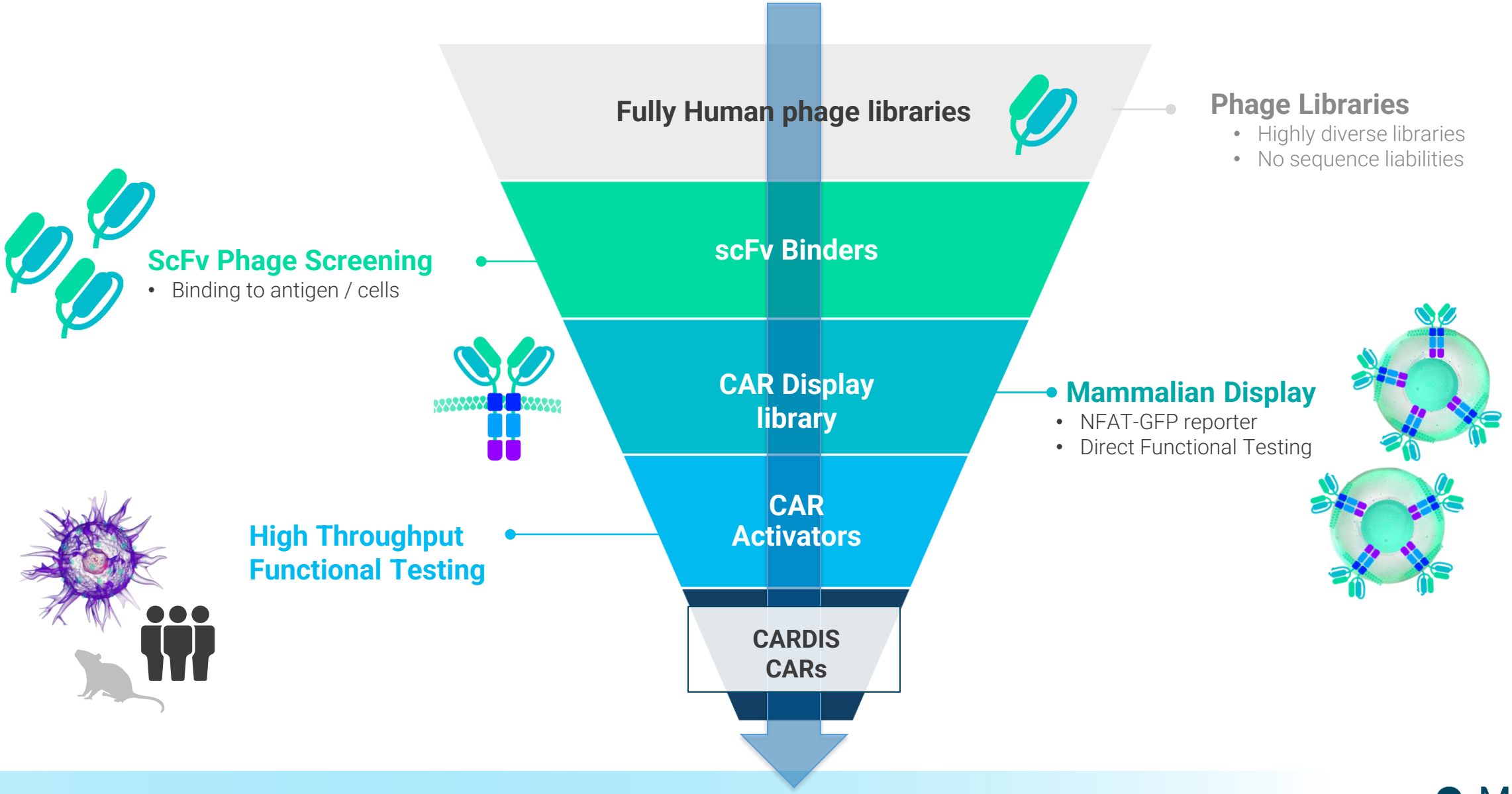
Functional components



CARDIS™ Platform
CARs to surface-expressed antigens



CARDIS Platform Enables Rapid Selection of Potent and Highly specific CARs

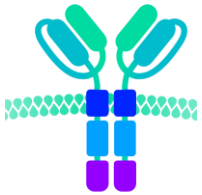


MiNK Therapeutics

CAR Display – the value-add step of CARDIS™

ScFv Phage Screening

- Binding to antigen / cells
- 2-3 weeks



High Throughput Functional Testing

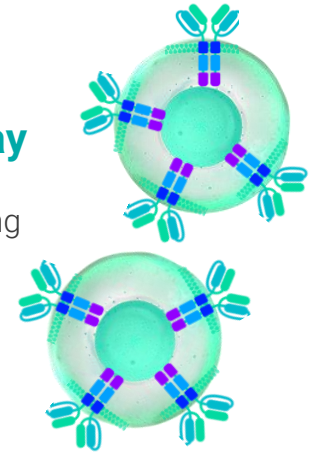
- Specific/non-specific activation
- Tonic signalling, mouse X-reactivity
- 4-8 weeks

Phage Libraries

- Highly diverse libraries (>10^{10})
- No sequence liabilities

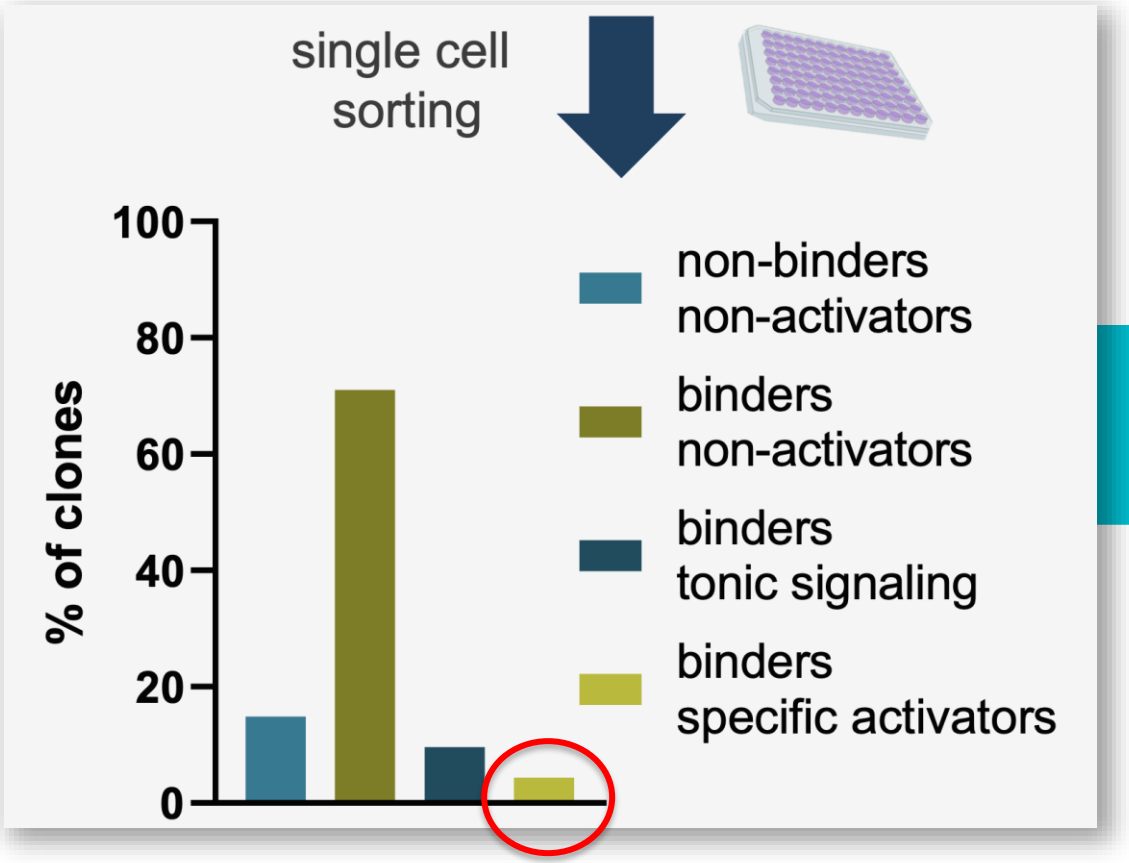
Mammalian Display

- NFAT-GFP reporter
- Direct Functional Testing



MiNK Therapeutics

CAR Display – the value-add step of CARDIS™



CAR library

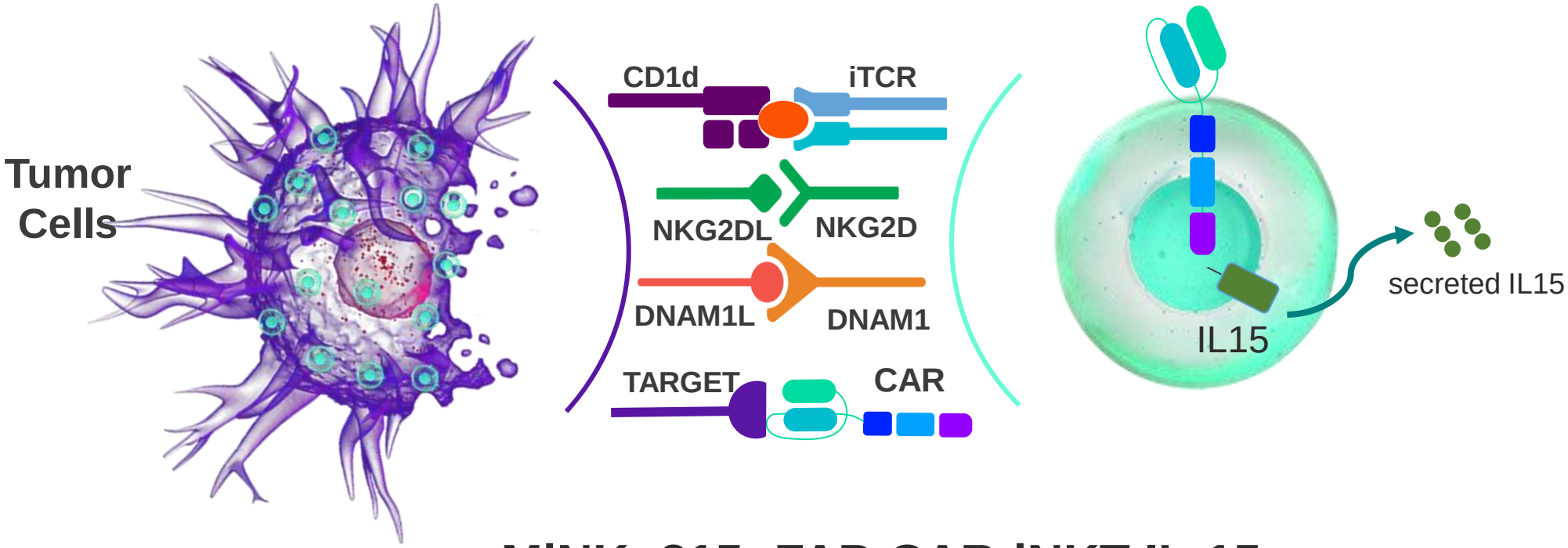
Mammalian Display

- NFAT-GFP reporter
- Direct Functional Testing

<1% of target binders make functional CARs – industry challenge

MiNK Therapeutics

MiNK CAR-iNKT portfolio – our most advanced programs



- **MiNK- 215: FAP-CAR-iNKT-IL-15**
- **MiNK- 413: BCMA-CAR-iNKT IL-15**

Adapted from: Wolf, B et al. Frontiers in Immunology. 2018

MiNK Therapeutics

Xavier Michelet, PhD

Associate Director of
Preclinical Immunobiology,
MiNK Therapeutics

MiNK Therapeutics

R&D DAY

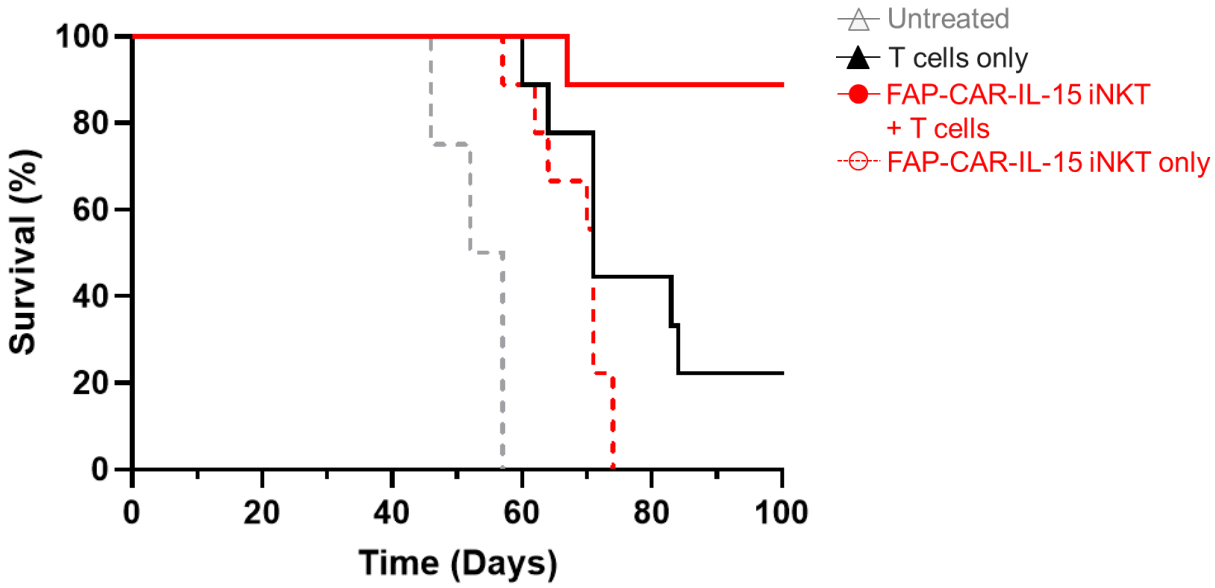
Abstract Number: 358

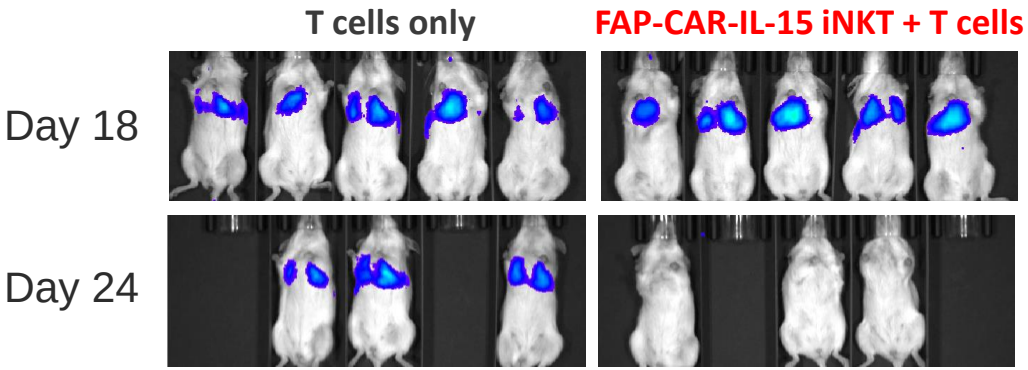
Development of an allogenic FAP-CAR-iNKT product to target tumor stroma and modulate the Tumor Microenvironment

MiNK FAP-CAR-IL-15 iNKT Cell Therapy Promotes Curative Responses in NSCLC Tumor-Bearing Mice

- MiNK FAP-CAR iNKT delays tumor engraftment through changing the tumor microenvironment and preventing tumor growth
- FAP-CAR-IL-15 iNKT appears to eliminate tumors more effectively than tumor specific T cells
- MiNK FAP-CAR iNKT promotes survival through enhancement of tumor-specific T cells activity
- MiNK FAP-CAR iNKT enhances infiltration and survival of tumor-specific T cells within the core of the tumor
- MiNK FAP-CAR iNKT has curative potential in one of the most prevalent and deadly cancer in which the immune system and PD-1 therapies are not enough
- MiNK FAP-CAR iNKT is a first of a kind product showing tremendous benefit toward a target widely expressed in lethal cancers

MiNK FAP-CAR-IL-15 iNKT Cell Therapy Promotes Curative Responses in NSCLC Tumor-Bearing Mice





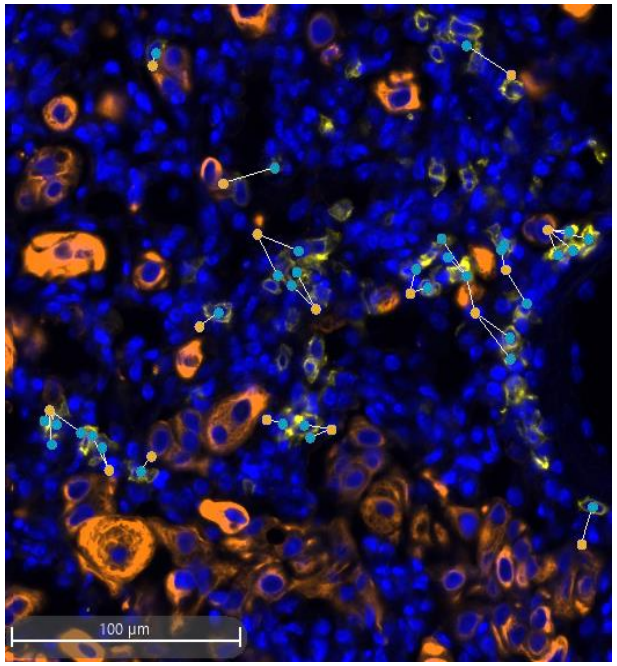
Lung tumor imaging

- NSCLC xenograft tumor model developing an immunosuppressive stroma resistant to tumor-specific T cell infiltration and activity
- FAP-CAR-IL-15 iNKT delays tumor engraftment in targeting the stroma that supports its growth
- 6 days post infusion, FAP-CAR-IL-15 iNKT treated lungs are mostly cleared while tumor specific T cells alone do not
- FAP-CAR-IL-15 iNKT promotes survival through enhancement of tumor-specific T cells activity

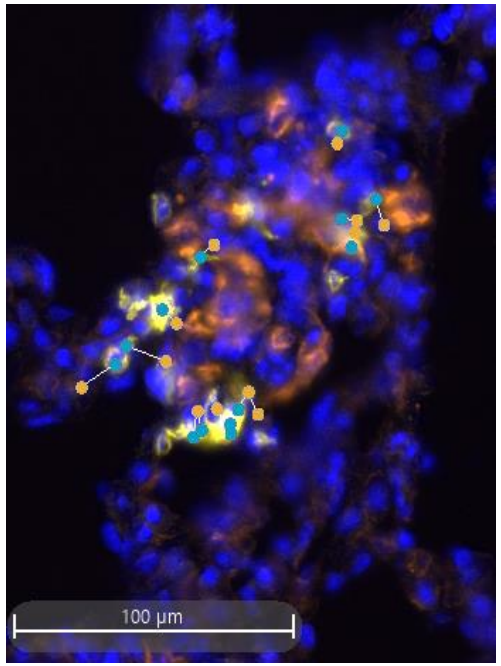
MiNK Therapeutics

FAP-CAR-IL-15 iNKT Enhances Infiltration of Tumor-Specific CD8+ T cells to Clear Tumor

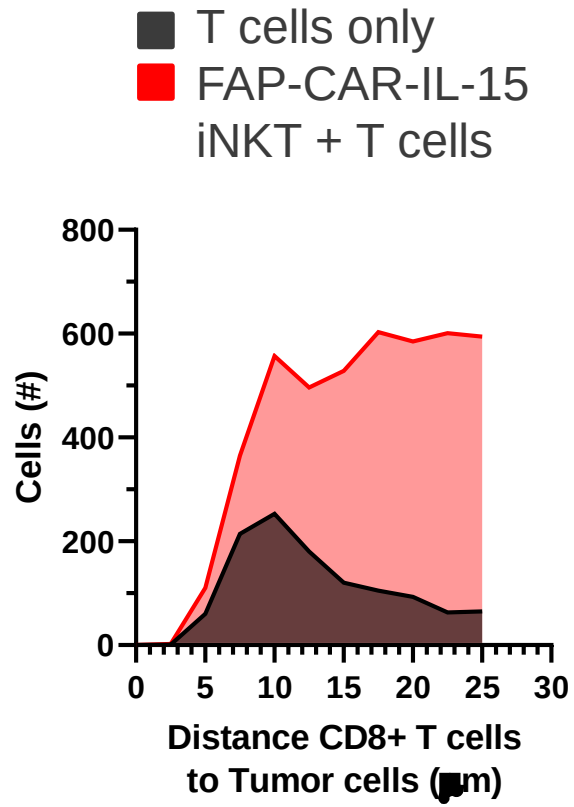
T cells only



FAP-CAR-IL-15 iNKT + T cells



Tumor cells
Tumor specific CD8+ T cells
Nucleus



- In absence of FAP-CAR iNKT, tumor-specific T cells remain excluded from the tumor core
- FAP-CAR-IL-15 iNKT cells increases the number of CD8+ T cells infiltrating the core of the tumor promoting tumor clearance

MiNK Therapeutics

Eleni Chantzoura, PhD

Director Discovery, MiNK

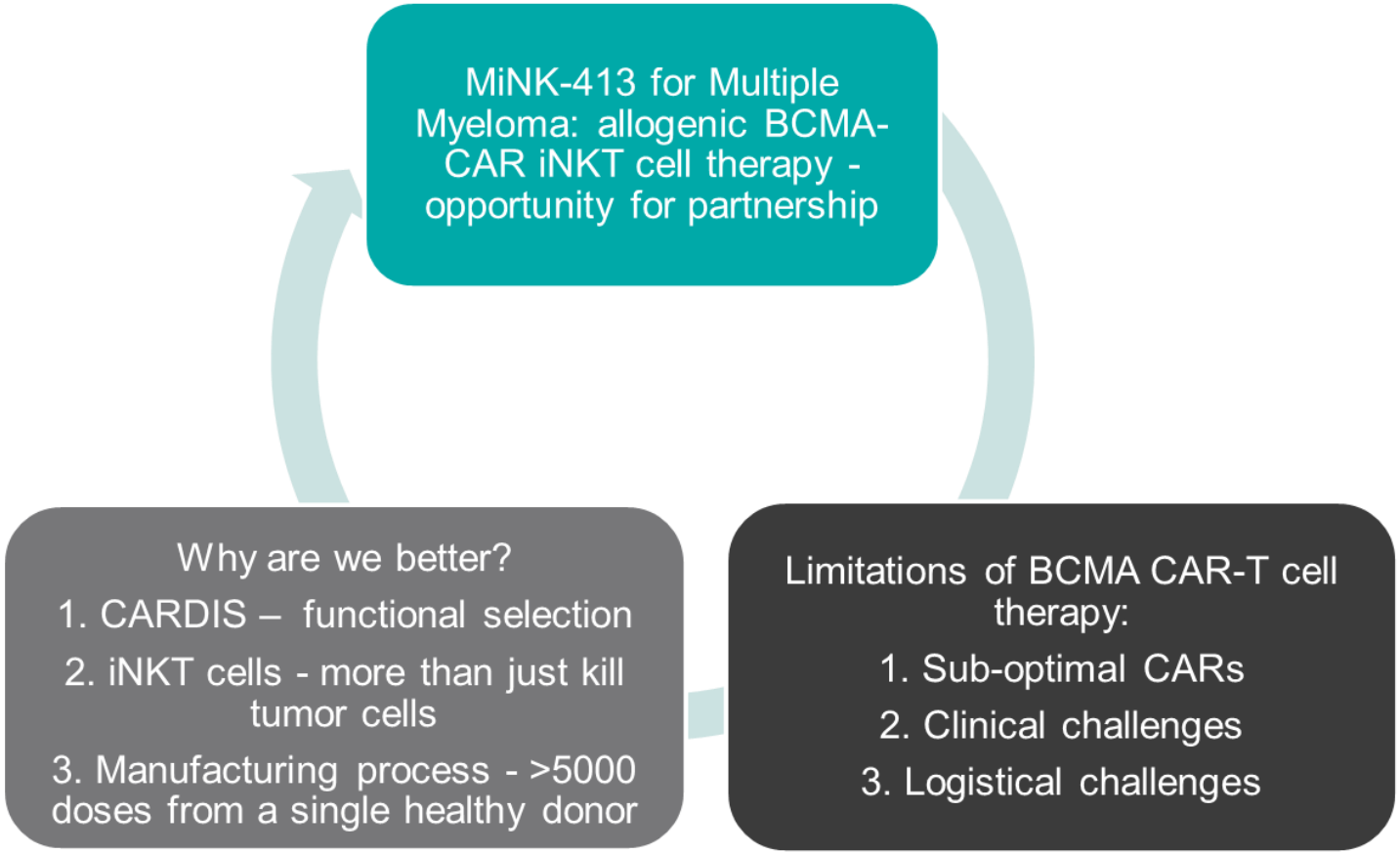
MiNK Therapeutics

R&D DAY

Abstract Number: 322

MiNK-413: a Next generation armored allogenic BCMA-CAR-iNKT product

MiNK-413: Not another BCMA CAR T-Cell Therapy

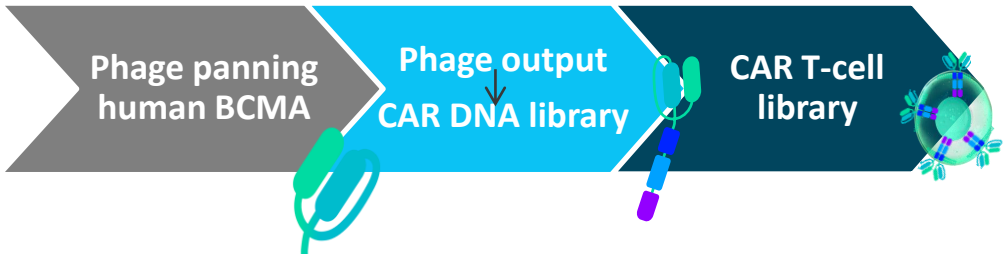


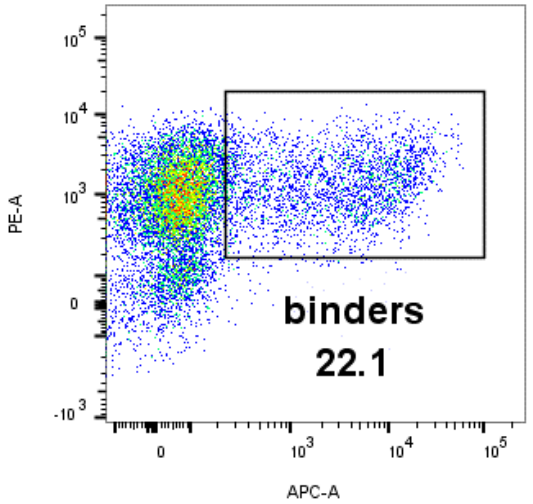
Therapy in Multiple Myeloma: Room for Improvement

- ❑ Sub-optimal CARs
- ❑ Clinical Challenges
- ❑ Manufacturing Limitations

MiNK Therapeutics

Sub-optimal CARs - Immunogenicity

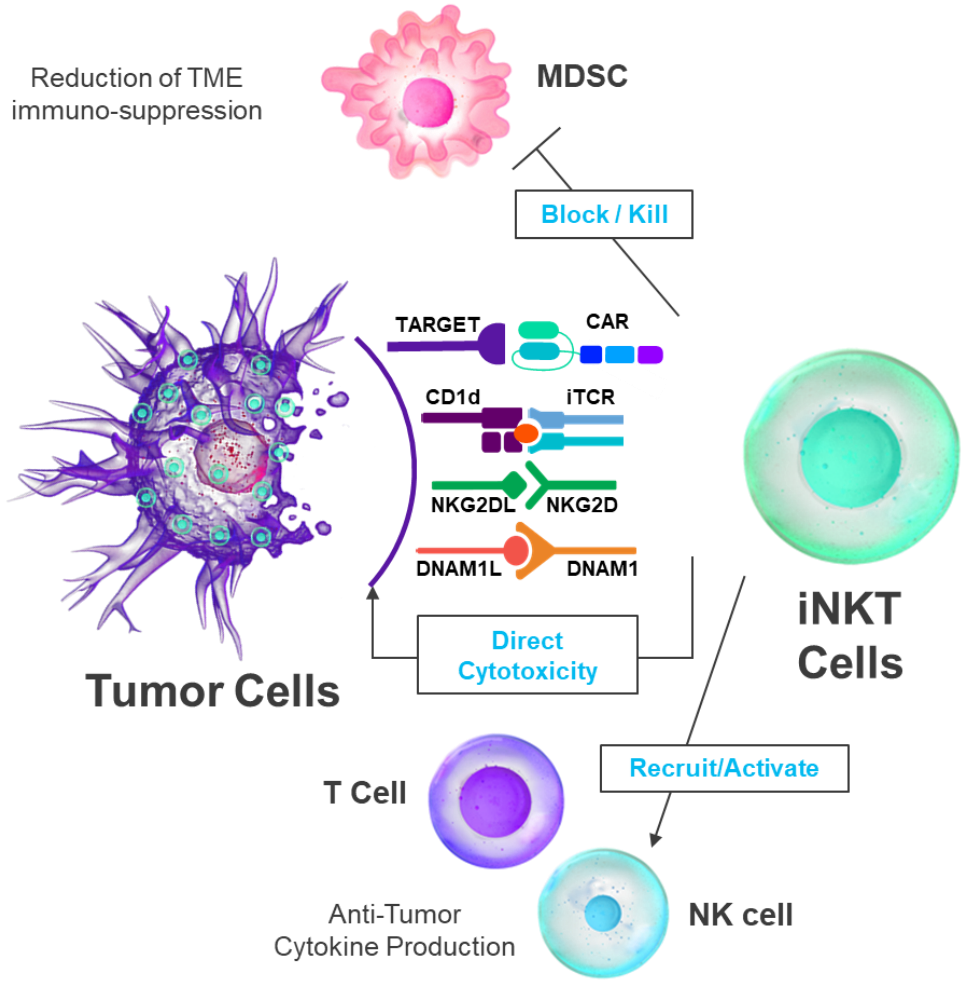




CARDIS: High-Throughput Identification of Functional CARs

MiNK Therapeutics

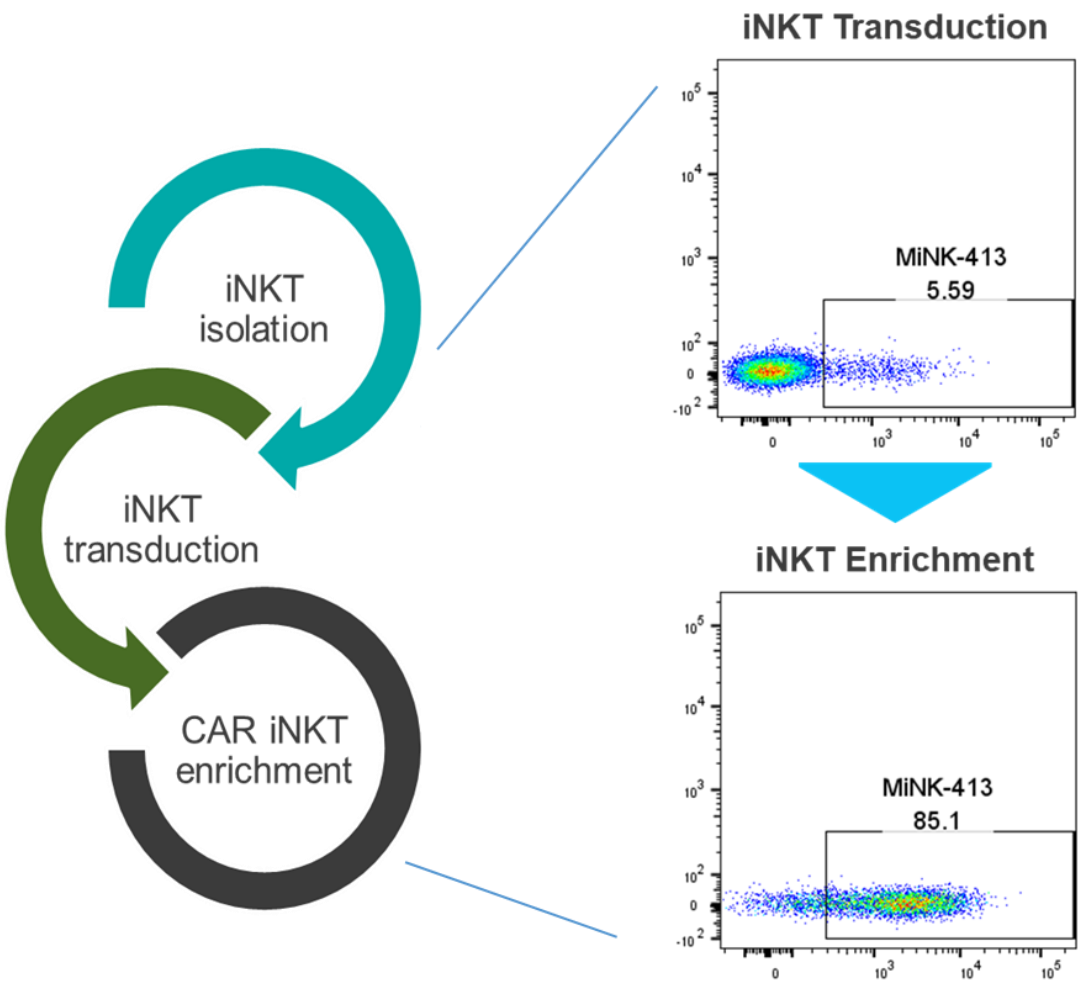
Clinical challenges – Multiple Myeloma is still incurable



BCMA CAR iNKT cells do more than just kill the tumor cells

MiNK Therapeutics

Manufacturing and Logistical Challenges

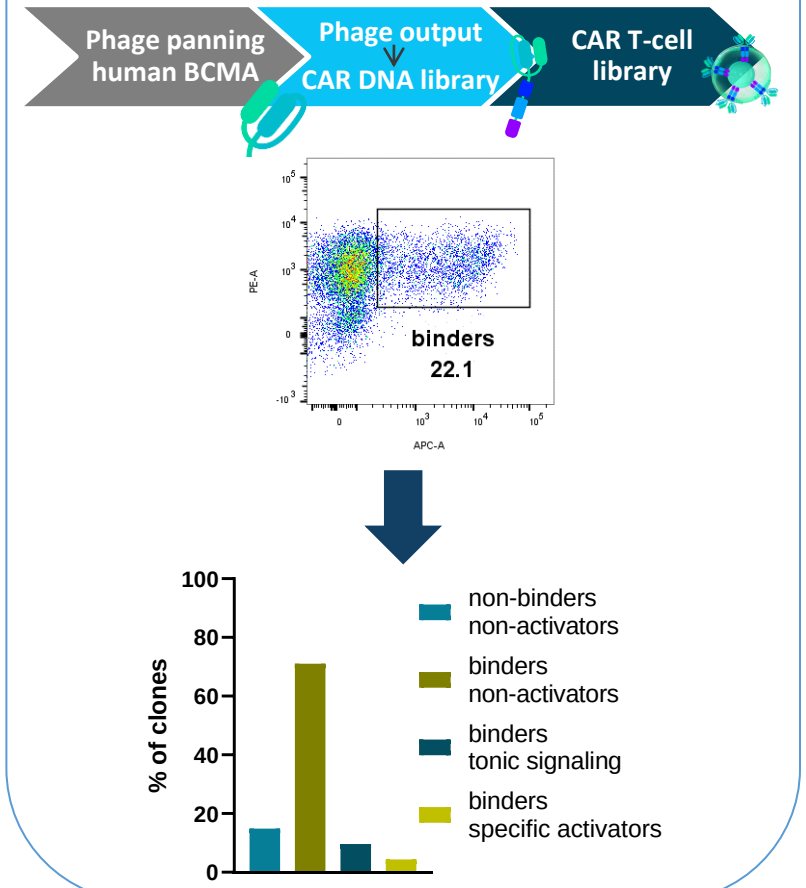


Up to 5000 doses from a single healthy donor

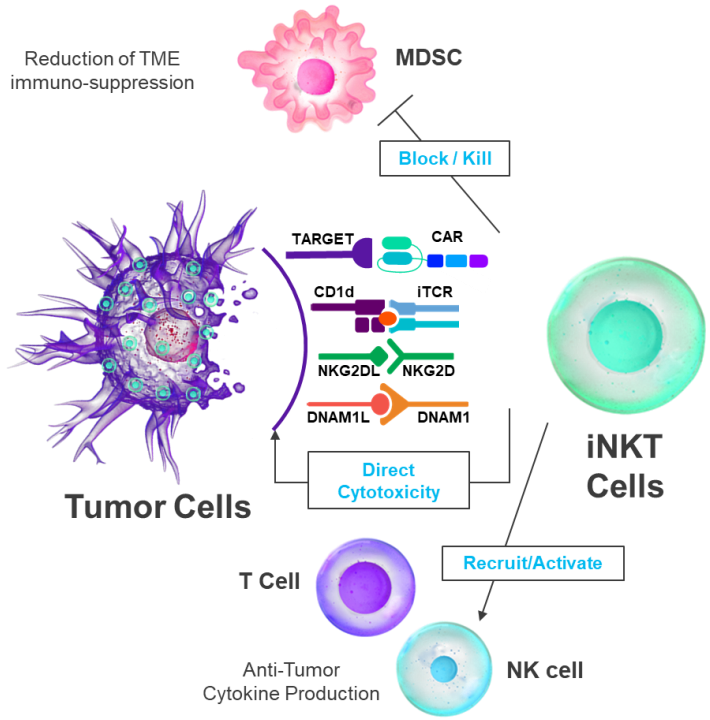
MiNK Therapeutics

MiNK-413: Not another BCMA CAR T-Cell Therapy

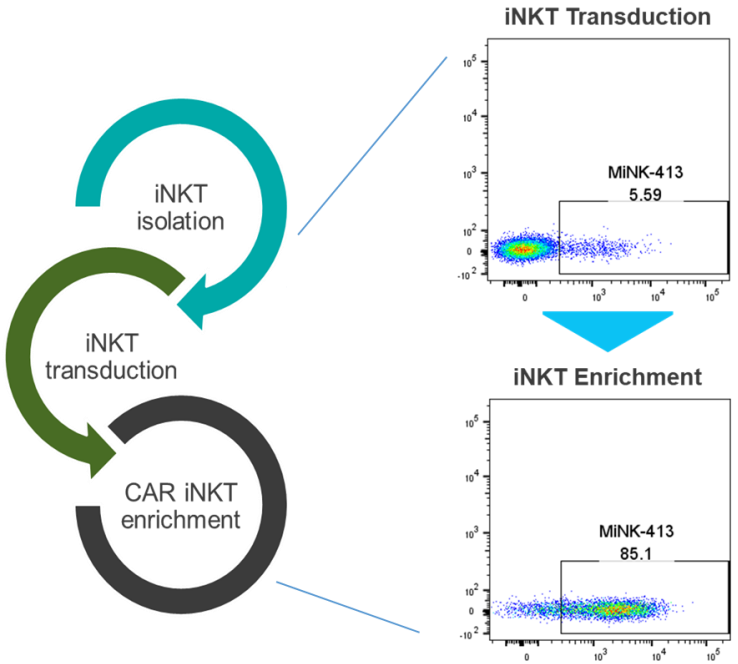
CARDIS: High-Throughput Identification of Functional CARs



BCMA CAR iNKT cells do more than just kill the tumor cells



Up to 5000 doses from a Single Healthy Donor



MiNK Therapeutics

MiNK Therapeutics

R&D DAY

Unlocking the constraints of cell therapy manufacturing to enable scalable, accessible, and affordable treatments

Joy Zhou, PhD

Head of CMC, MiNK Therapeutics

Curative Efficacy of Cell Therapy with Rapid Accessibility and Affordability

*MiNK unlocks constraints of cell therapy large scale manufacturing to enable an **accessible** and **affordable** treatment*

Available Autologous Cell Therapy Dynamics

Cost of Goods (per treatment):
>$500K per patient*

Production Scalability:
1 batch = 1 patient **

Availability (from qualification of treatment to time treatment is delivered):
2-3 months ***

* recently approved SKYSONA from Bluebird bio to treat CALD (active cerebral adrenoleukodystrophy) priced at $3M per dose
** a batch is a single production run that typically spans 3-4 weeks
*** when a patient requires the treatment, there needs to be a production run followed by release, which together take 10-12 weeks)

MiNK Allogeneic Cell Products

Target cost of Goods (per treatment):
≤$10K per patient*

Production Scalability:
1 batch ≥5,000 patients*

Availability (from qualification of treatment to time treatment is delivered):
<1 day**

* includes release, packaging, labeling, etc. – we expect to achieve these COGS and production scale levels in 2024 based on 300M cells per dose
** our product will be available off the shelf as a cryopreserved product

MiNK Therapeutics

Internal Manufacturing Path to Achieve ≥700,000 DOSES PER YEAR

We've designed production capacity with commercial ready mfg suite to produce ≥ 700,000 doses/year production potential

Cell expansion
(2-3 weeks)

Harvest & Purification
(<1 day)

Formulating & Fill/Finish
(< 1 day)

Proprietary reagents for INKT purification; proprietary process for INKT activation
Estimated 3-week manufacturing time and 5,000 doses per batch is designed to achieve ~600-700,000 doses per year

MiNK Therapeutics

Dr. Terese Hammond

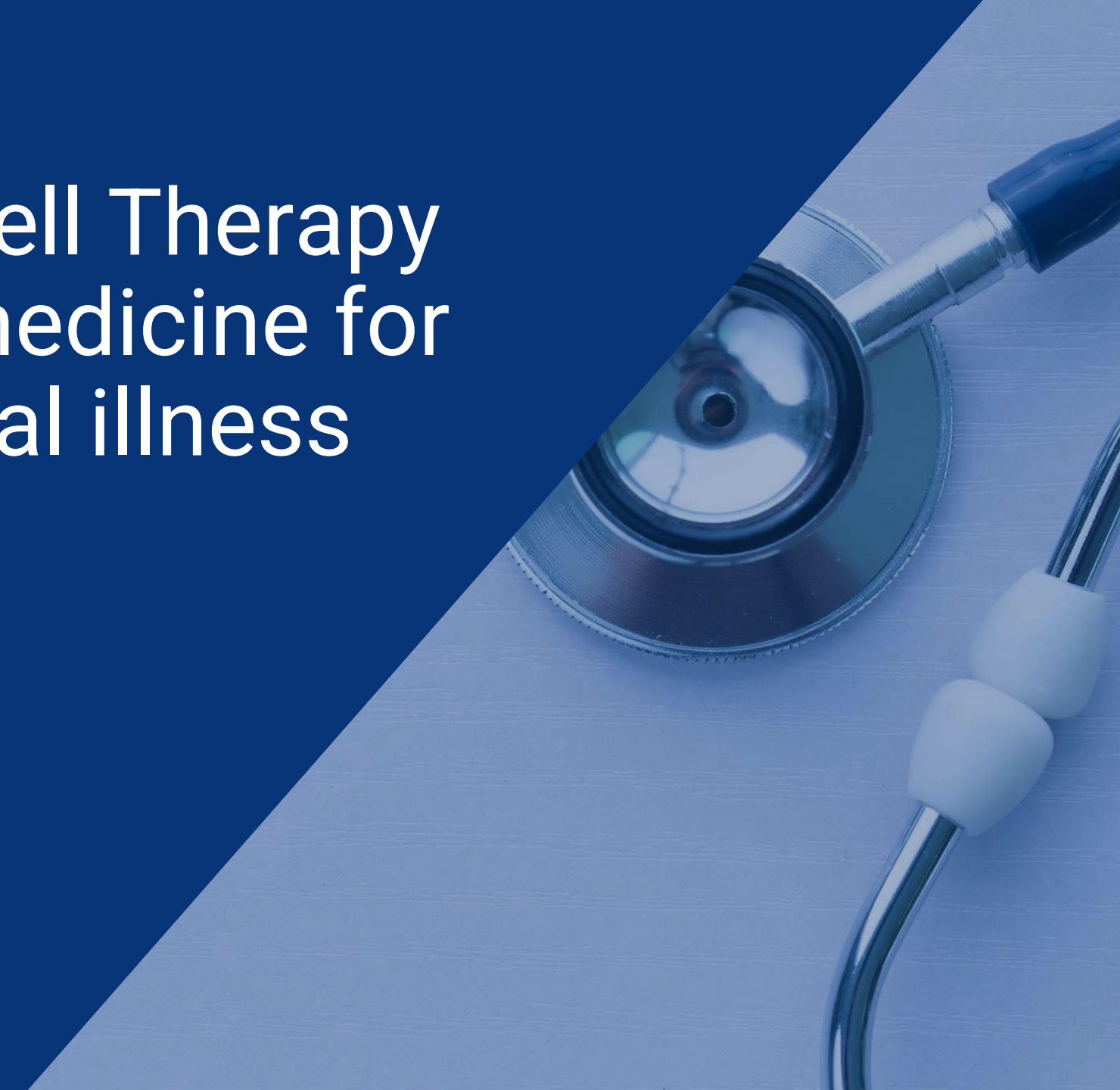
- Program Medical Director, Providence Saint John's Health Center and pulmonary critical care expert
- Pioneering work in clinical and translational science in critical care of COVID-19

Saint John's Cancer Institute

Saint John's Health Center

Providence

The Future of Cell Therapy and precision medicine for ARDS and critical illness



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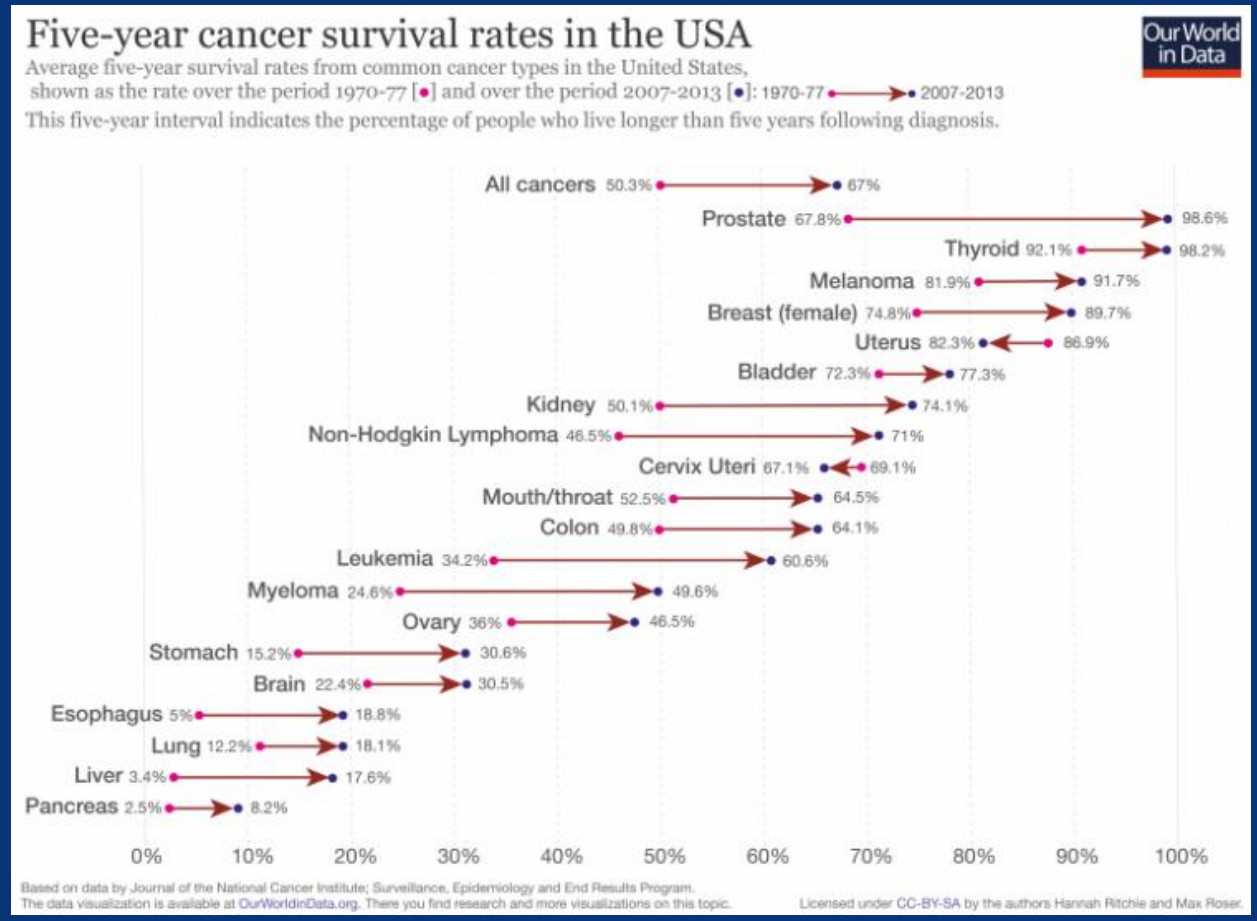
Mortality of Critical Illness Exceeds Most Cancers

- Mortality Rates
  - Sepsis: 25-50%
  - ARDS: 35-45%
  - COVID-19: 30.9% overall and 35.7% mechanically ventilated
  - COVID-19 ECMO: 40-70%
  - Ruptured AAA: 80%
  - SAH: 20-50%



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https://ourworldindata.org/cancer-death-rates-are-falling-five-year-survival-rates-are-rising

iNKT Development in ARDS and Viral Infections

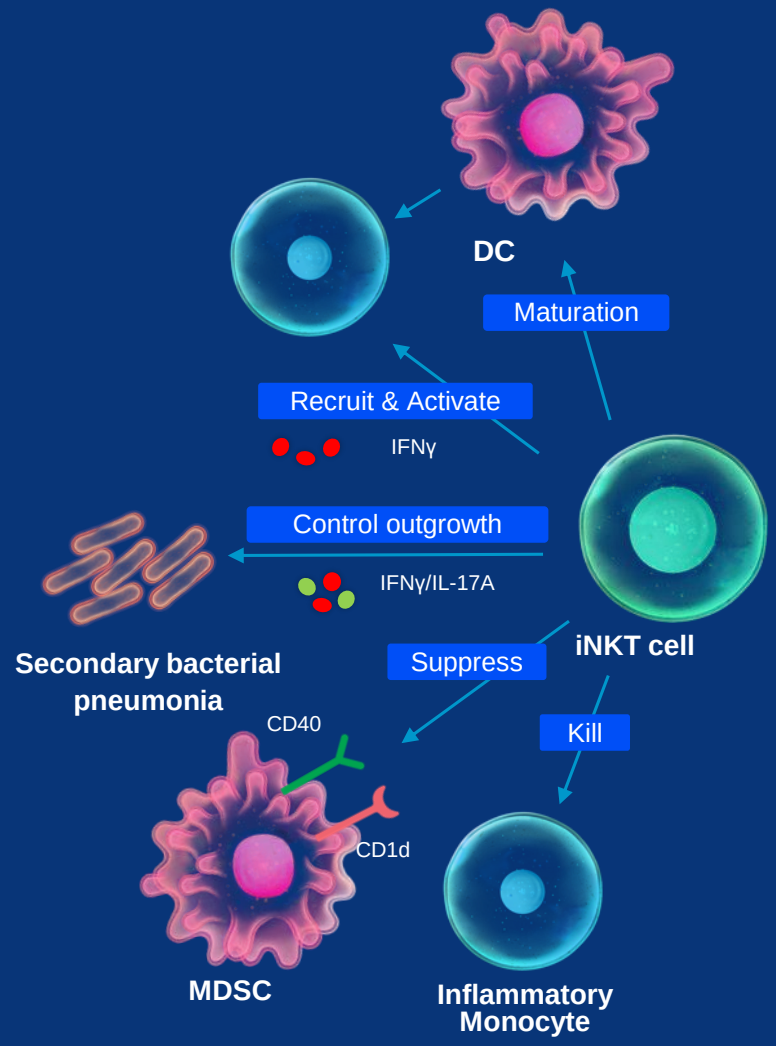
Versatile & critical cells for suppressing inflammatory cytokines, fighting infection, and reducing relapse in patients

Acute Respiratory Distress (ARDS)

Acute respiratory distress syndrome (ARDS) is inflammation driven respiratory failure in COVID, Flu, Sepsis and other infections

ARDS represents nearly 1M patients in ICU and 40% die

iNKTs home to lung, dampen inflammatory cytokines (IL-1 & IL-6), clear virus, and may prevent reinfection



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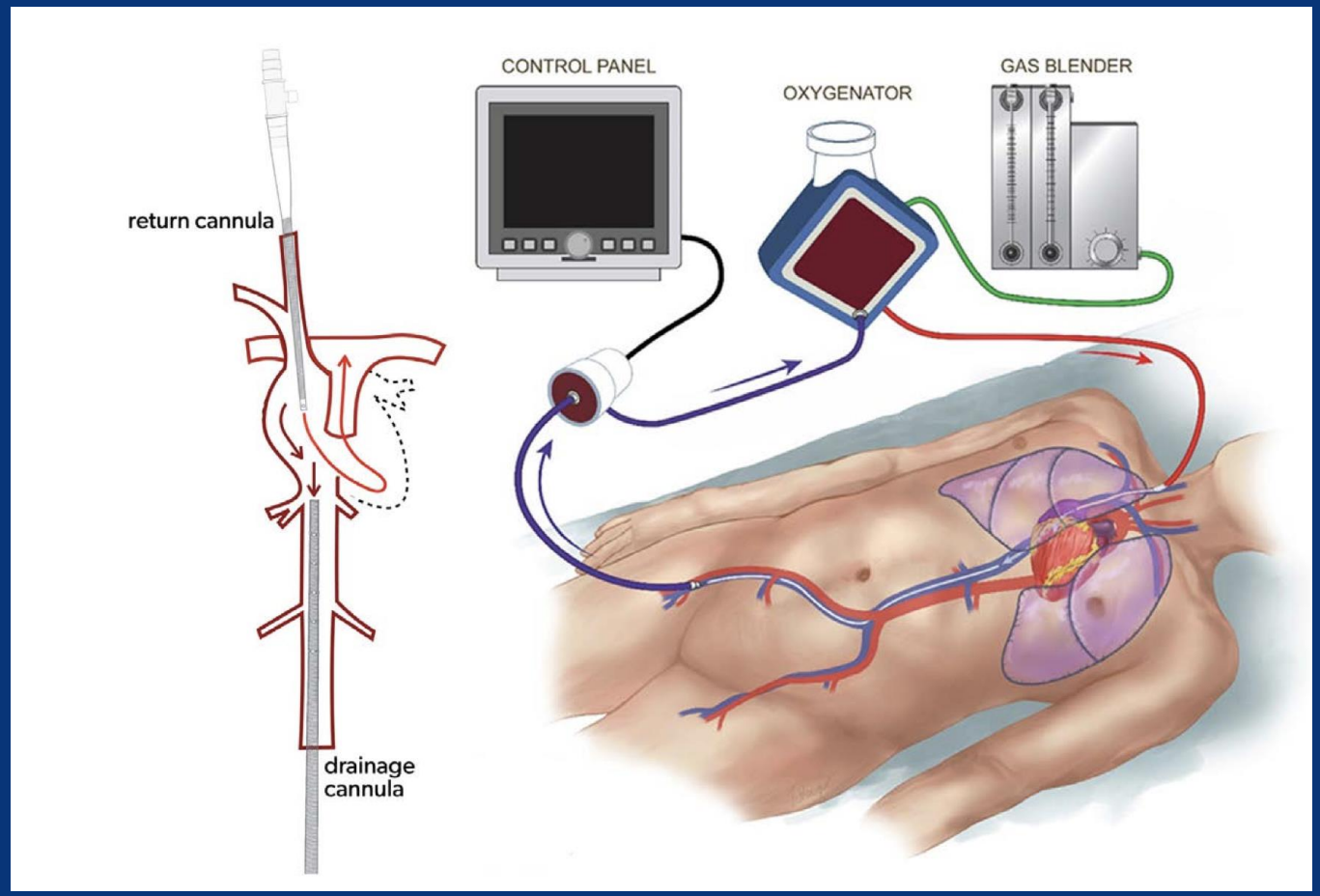
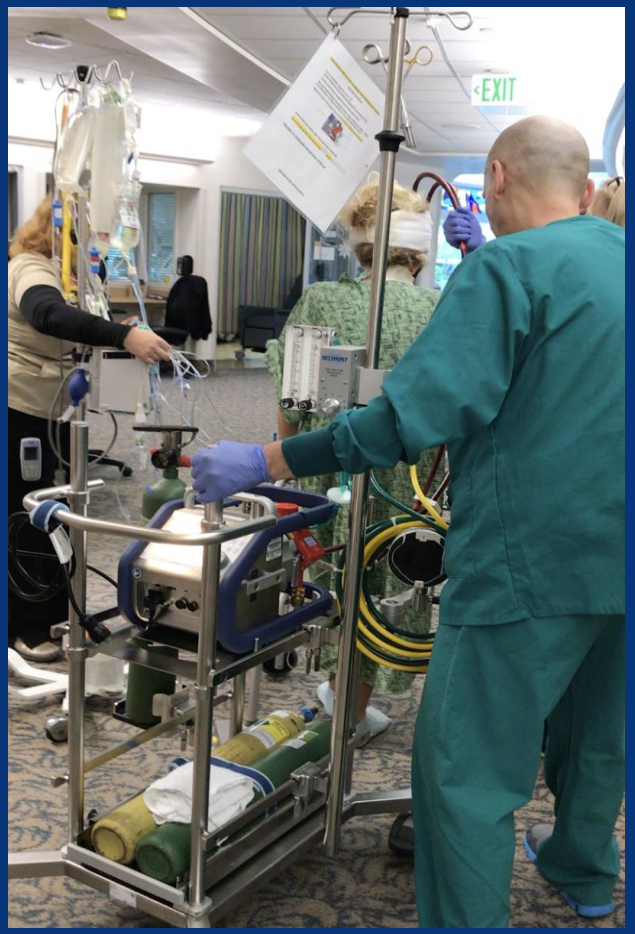
VV-ECMO is LUNG BYPASS





Saint John's Cancer Institute
Saint John's Health Center
Providence

Gajkowski, Evan F., et al. "ELSO guidelines for adult and pediatric extracorporeal membrane oxygenation circuits." *ASAIO Journal* 68.2 (2022): 133-152.

agenT-797 (allogeneic unmodified iNKTS) in subjects with moderate to severe acute respiratory distress syndrome (ARDS) secondary to SARS-CoV-2 (COVID-19)

- All participants to receive a single infusion of agenT-797 in doses of 100, 300, 1000, × 10^6 cells
- Subjects were eligible if they were infected with a diagnosis of moderate to severe ARDS secondary to SARs-Cov-2 or influenza per Berlin Definition (2012)

Patient Demographics

Variable	Cohort 1	Cohort 2	Cohort 3	Total
agenT-797 dose level (cells)	100 X 10^6	300 X 10^6	1000 X 10^6	
Subjects dosed (n)	3	4	13	20
Age				
Median (range)	67 (66-77)	71.5 (64-75)	62 (26-75)	66.5 (26-77)
Sex, n (%)				
Male	2 (66.7)	1 (25.0)	7 (53.8)	10 (50.0)
Female	1 (33.3)	3 (75.0)	6 (46.2)	10 (50.0)
Patient disposition				
Early Discontinuation	0	1 (25.0)	5 (38.5)	6 (30.0)
Death	0	1 (25.0)	5 (38.5)	6 (30.0)

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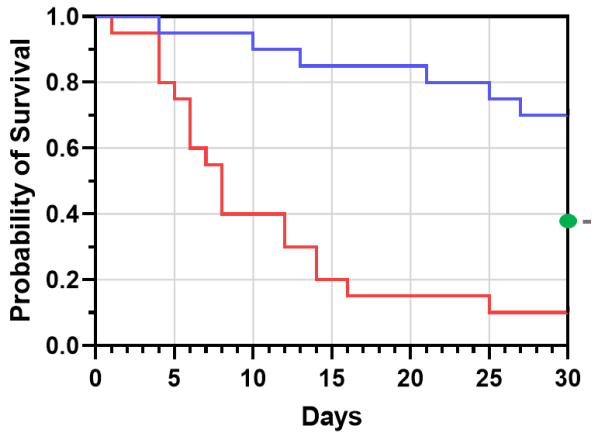
agenT-797 Shows Improved Survival and Favorable Safety Profile in Severe ARDS

70% Survival Compared to 10% Case Control



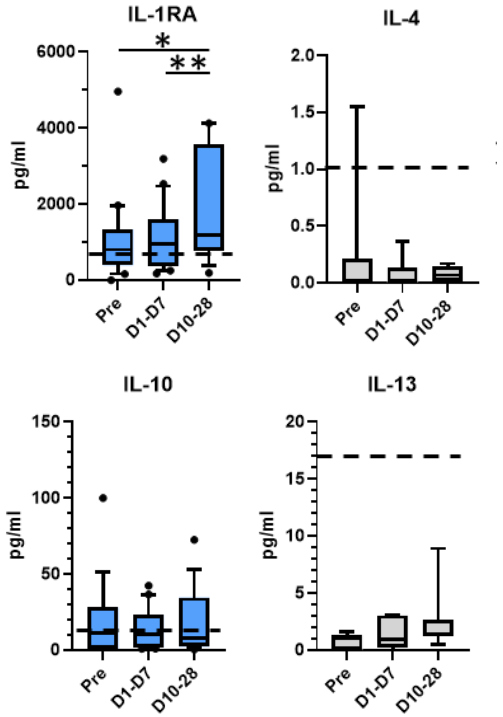
agenT-797

Comparative control

Reduced Incidence of Secondary Infections, including Pneumonia

N (%)	Dose Level 1 (n=3)	Dose Level 2 (n=4)	Dose Level 3 (n=13)
Pneumonia	**2 (67)**	**3 (75)**	**2 (15)**
Bacteraemia	2 (67)	0	1 (8)
Urinary tract infection	0	3 (75)	1 (8)
Fungaemia	0	1 (25)	1 (8)
Cytomegalovirus viraemia	0	0	1 (8)
Lung abscess	1 (33)	0	0
Pneumonia klebsiella	0	1 (25)	0
Sepsis	1 (33)	0	0
Septic shock	0	0	1 (8)
Upper respiratory tract infection	1 (33)	0	0

Increased Anti-Inflammatory Response



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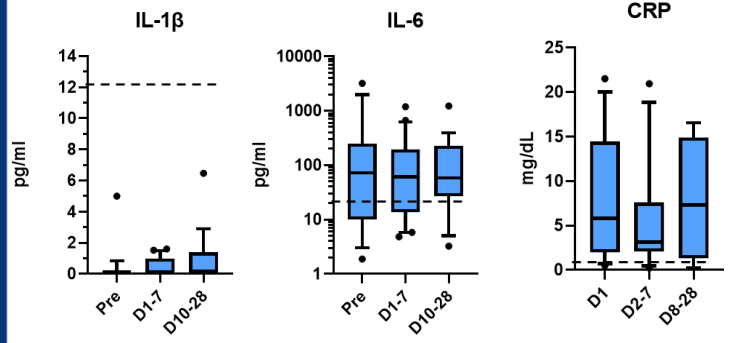
agenT-797 is Well Tolerated With Potential for Redosing

No DLTs and Few Related AEs

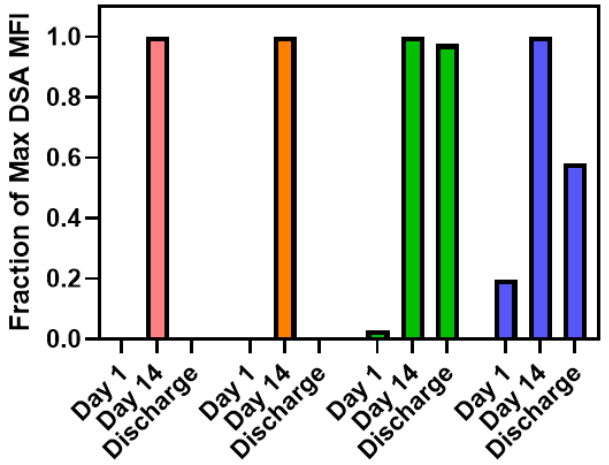
N (%)	All doses (n=20)
Any AE grade ≥ 3	19 (95)
Any TRAE grade ≥ 3	1 (5)
Any TRAE leading to discontinuation	0 (0)
Any TRAE leading to dose interruption	0 (0)
Any TRAE leading to death	0 (0)

- Most TEAEs were grade 1, 2 and consistent with severe Covid19/ARDS (anemia, fever, acute kidney injury)
- One grade 4 TRAE of dyspnea

No Cytokine Release Syndrome



Transient Antibody Response Suggests Redosing Potential



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INKT Therapy Shifting the Paradigm for Critical Infections

- Severe lung infections induce hyper-inflammation causing life-threatening disorders
- iNKT cells improve the disease course in severe viral infections of the lung
  - Destroy immunosuppressive MDSCs
  - Improve anti-viral immune responses
  - Reduce injury of the lung by limiting infiltration of inflammatory monocytes
  - Aid the clearance of viral infection-associated secondary bacterial pneumonia
- In severe COVID-19 the activation level of iNKT cells is predictive of clinical outcomes
- iNKT cells show resilience in the face of therapeutic steroids (dexamethasone in COVID-19) and potentially other immunotherapies (Cellcept in lung transplantation)
- Observations suggest that INKTs are “intelligent”; customizing a local response on contact

MiNK Therapeutics

R&D DAY

agenT-797 Biosignatures in Solid Tumors and COVID-19/ARDS

Marco Purbhoo

Director Translational Research
MiNK Therapeutics

agenT-797 Biosignatures in Solid Tumors and COVID-19/ARDS

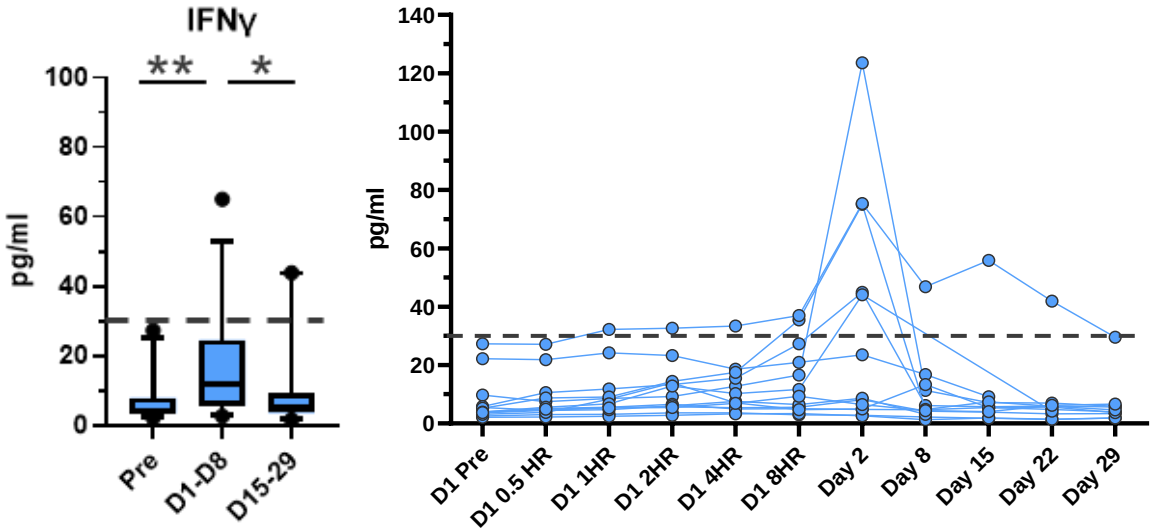
- agenT-797 represents a balanced iNKT cell-based drug product capable of responses across the pro- and anti- inflammatory spectrum

- In solid tumors an anti-inflammatory tumor microenvironment suppresses immune cell infiltration and activation
  →Pro-inflammatory iNKT response

- In viral-associated ARDS dysregulated hyperactivated immune responses result in acute injury of the lung
  → Anti-inflammatory iNKT response

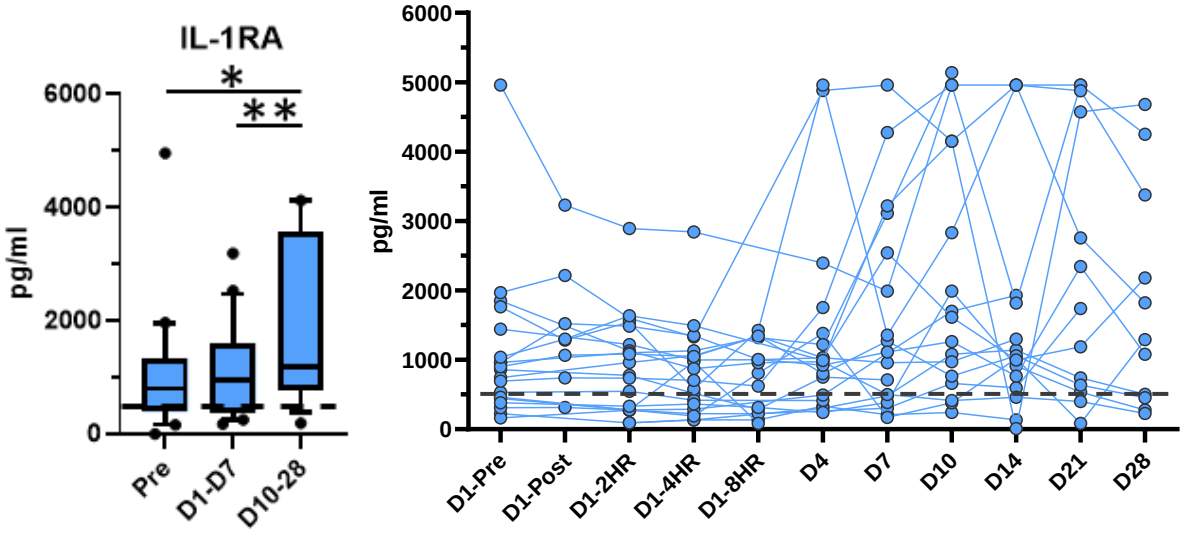
agenT-797 Biosignatures in Solid Tumors and COVID-19/ARDS

agenT-797 shows Pro-inflammatory signature in patients with Solid Tumors



Detection of key iNKT cell effector cytokine (IFNγ) consistent with rapid iNKT activation in the solid tumor setting and initiation of iNKT driven Th1 immune responses, including Dendritic cell activation and T cell/NK cell tumor recruitment.

agenT-797 shows anti-inflammatory signature in patients with ARDS



Enhancement of key anti-inflammatory cytokine (IL-1RA) levels suggests activation of mechanisms to downregulate the dysfunctional, hyperactivated immune response underlying viral-associated ARDS.

MiNK Therapeutics

Lydia Lynch, PhD

Scientific Advisory Board Member, MiNK

- Director of the Metabolic Core and Principal Investigator of Lynch Lab Harvard Medical School.
- Associate Professor of Medicine, Brigham and Women's Hospital, Harvard Medical School.

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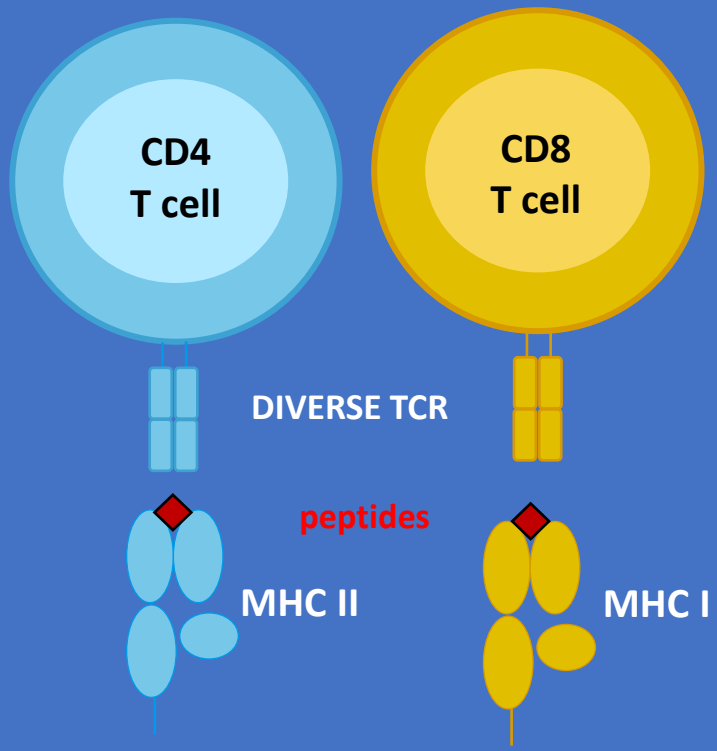
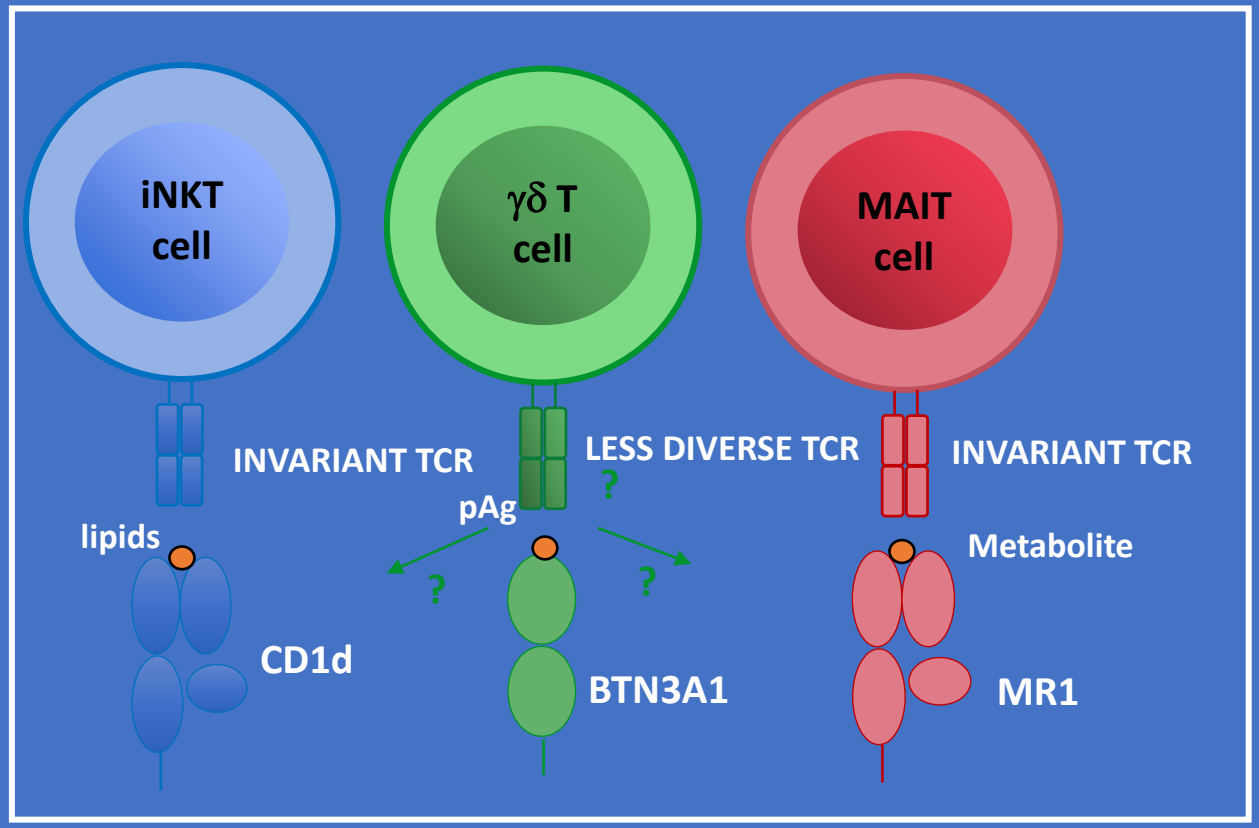
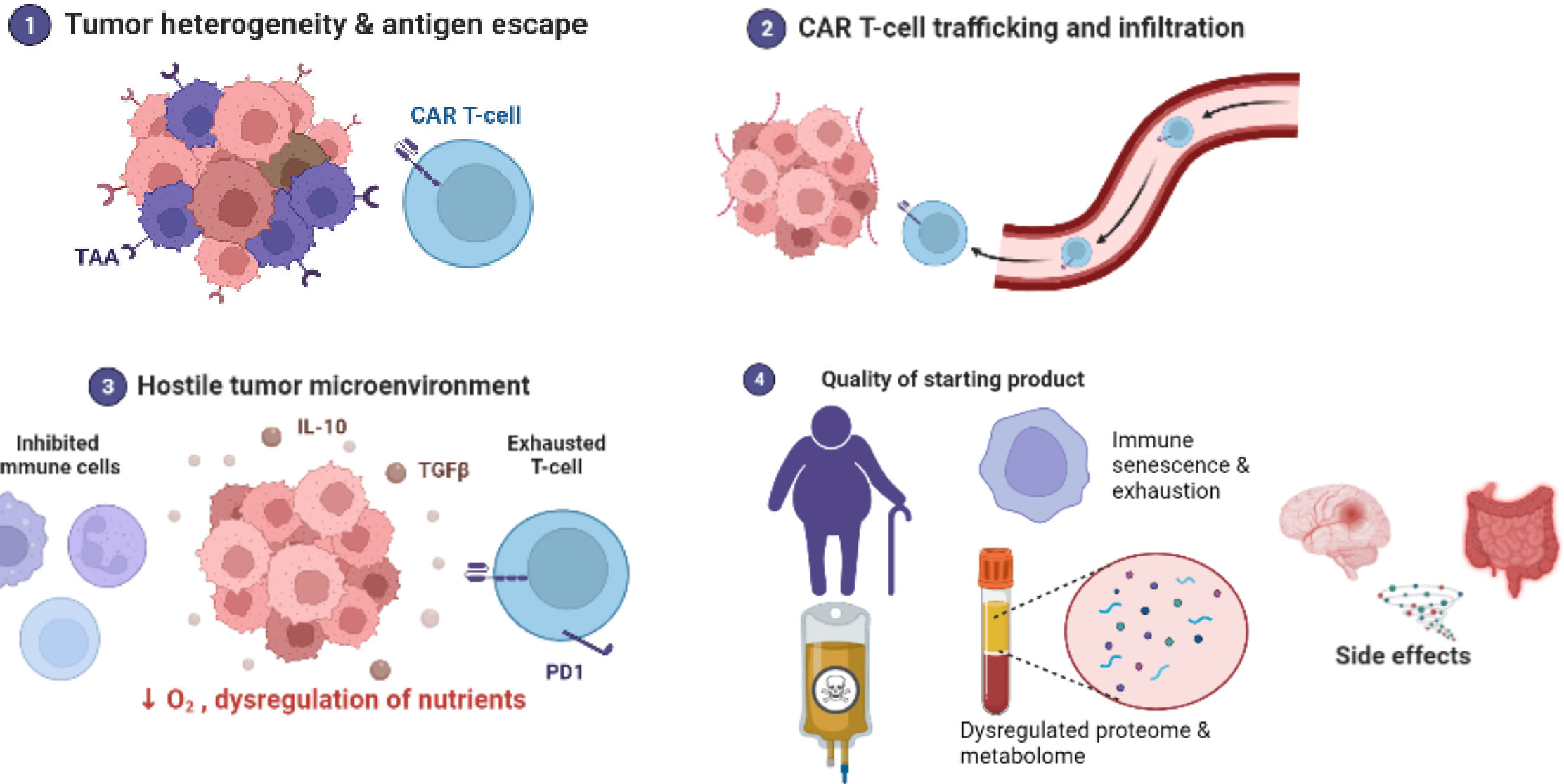
The Key Drivers and Regulators of Immunity – a Perspective

Innate T cells are an unappreciated, and understudied regulator in the body





Some reasons for limited success of ACT for solid tumors



Features that make innate T cells a preferred choice for adoptive cell therapy

- Not MHC restricted
- Recognize stress
- Tissue resident
- Not circulating

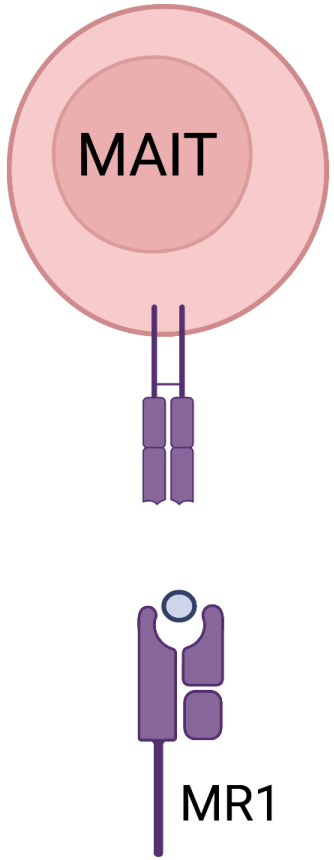
✓ No GVHD, Off the shelf therapy

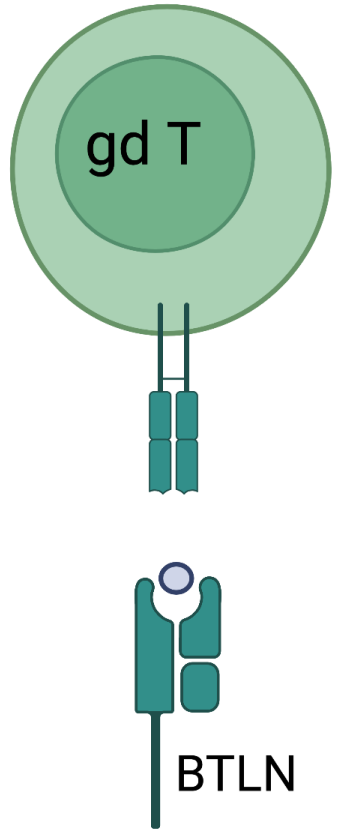
✓ No need to know antigen

✓ Natural homing to tissue

✓ Suited for the metabolic environment of tissue

Which innate T cell is best? Unbiased competition





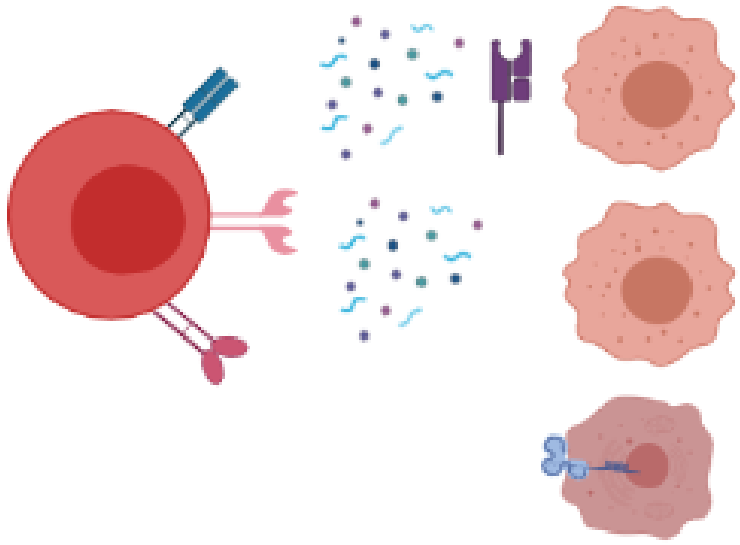
Can kill in vivo
Help other cells kill
Known antigen – can expand

Can kill
Can produce IL-17 in tumors
May require antigen
Limited expansion

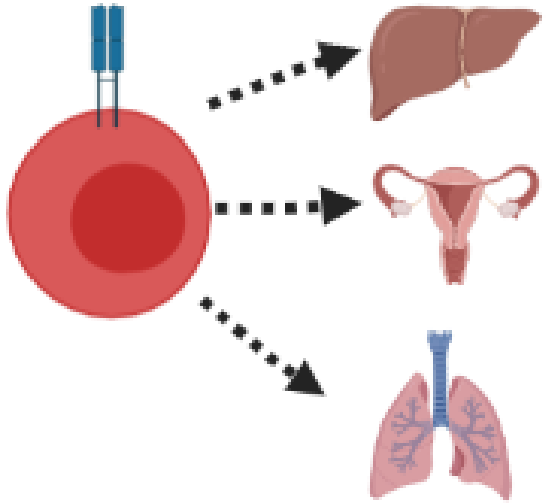
Can kill
No IL-17 in human tumor
Dont require antigen
Limited expansion

iNKT cells naturally address problems with current ACT

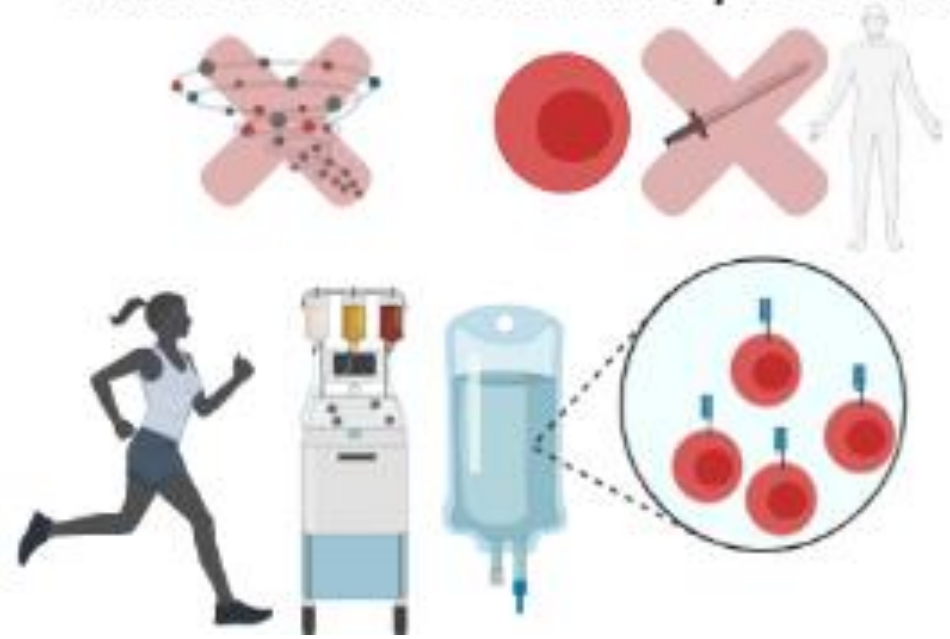
Recognise a range of targets



Naturally home to tissues



Limited side effects & mass production



iNKT cells naturally address problems with current ACT

MiNK Therapeutics have demonstrated how iNKT cells are an excellent choice for immunotherapy.

They have proven that their inherent features that we long suspected would be beneficial for ACT, actually are

How might we make them even better?

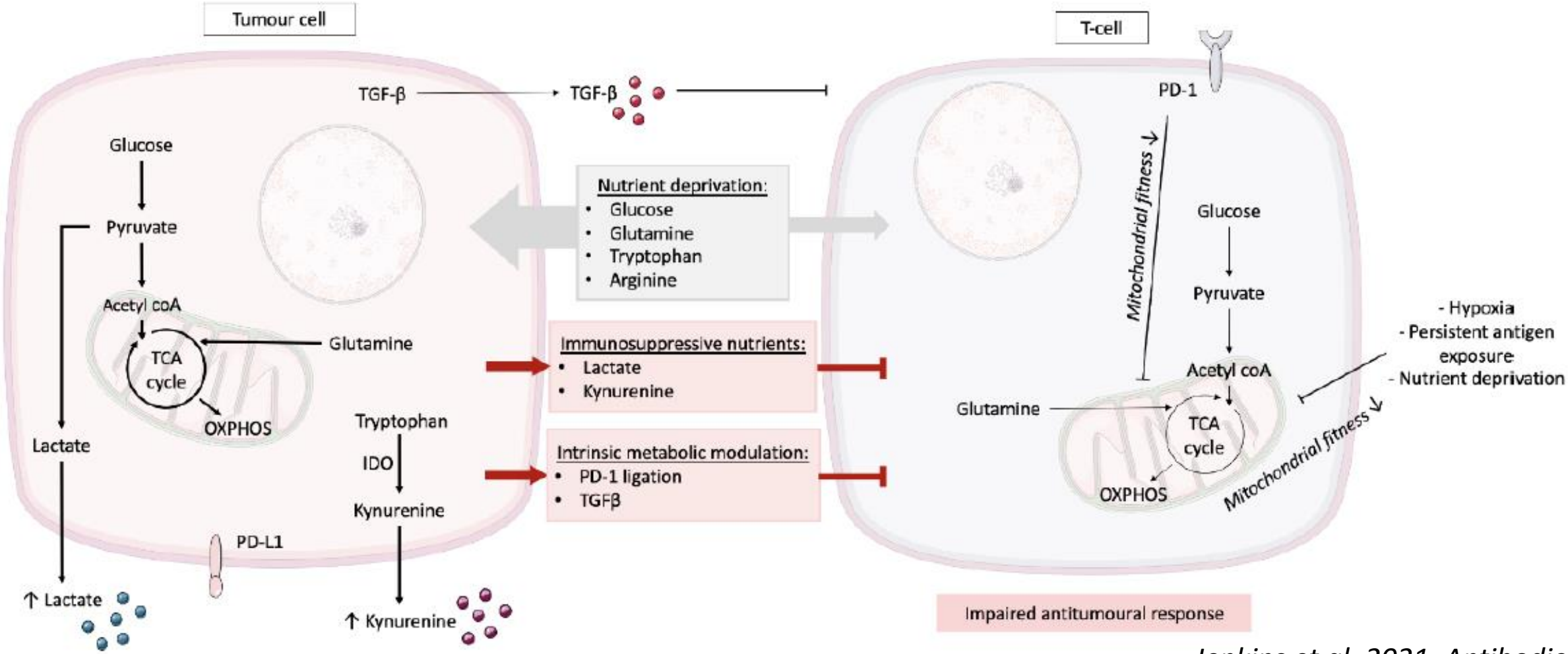
MiNK FAP-CAR-IL-15 iNKT Cell

BCMA CAR iNKT-Cell

CARDIS™ Platform

Future Approach: Metabolic Reprogramming

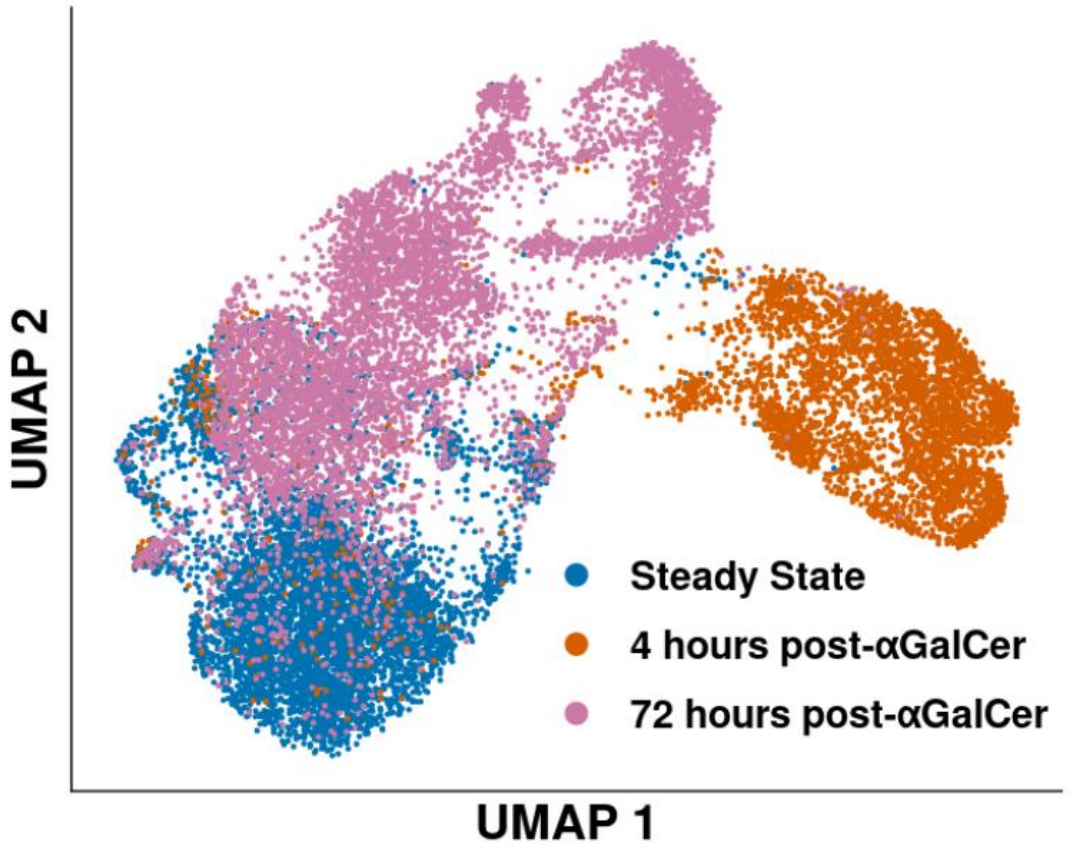
Mitochondrial fitness essential for tumor activity

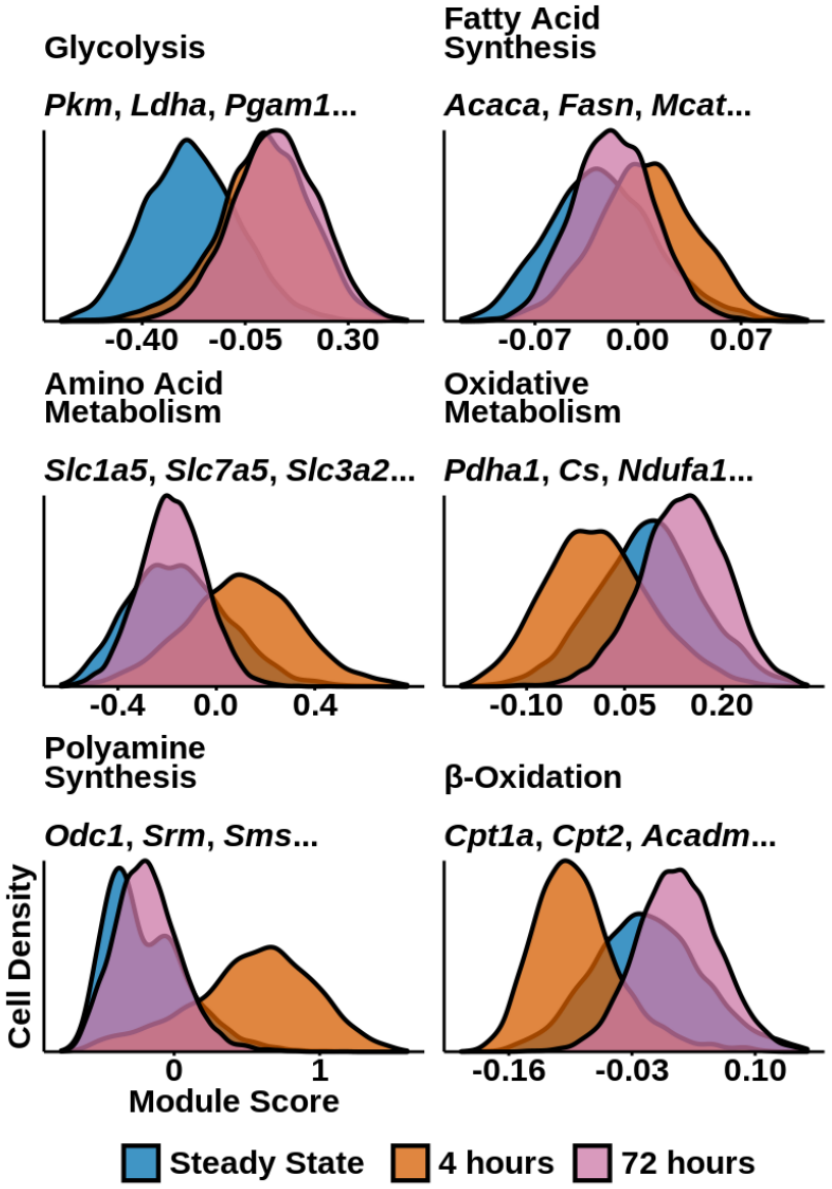


Jenkins et al. 2021, Antibodies

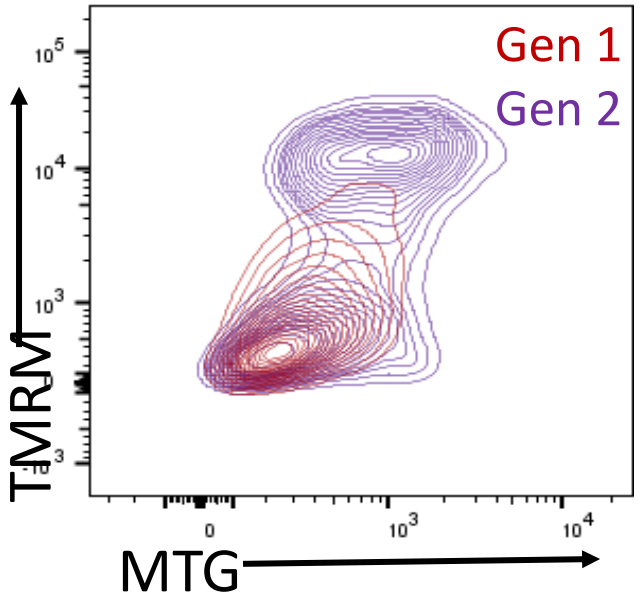
Transcriptional and metabolic programs associated with iNKT subsets and states

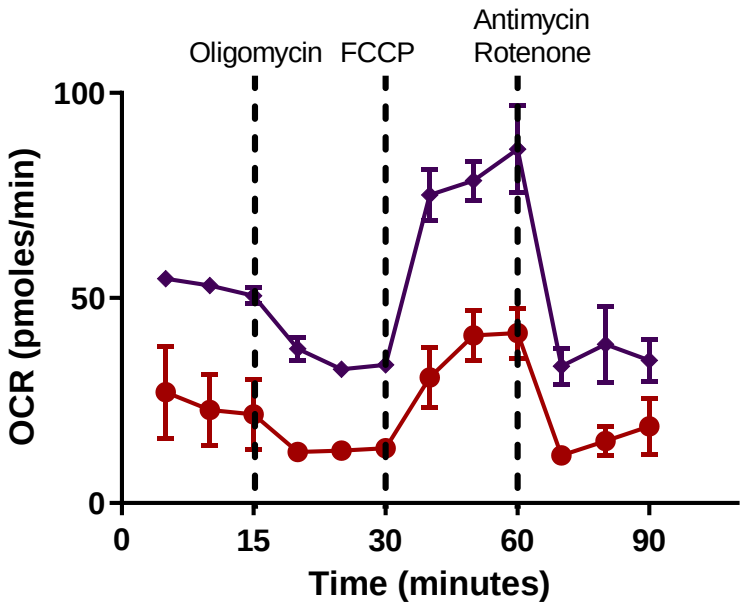
scRNA Seq - 16,500 iNKT cells

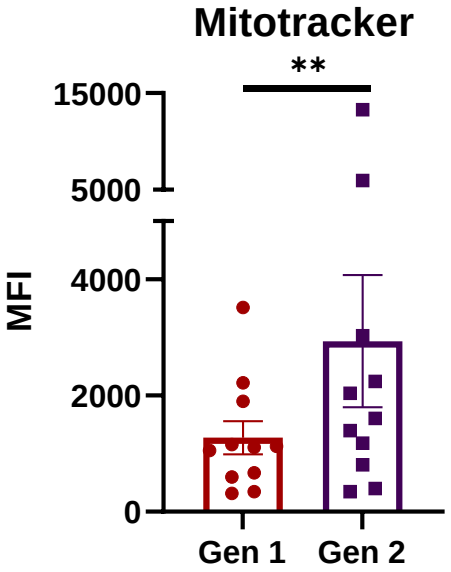


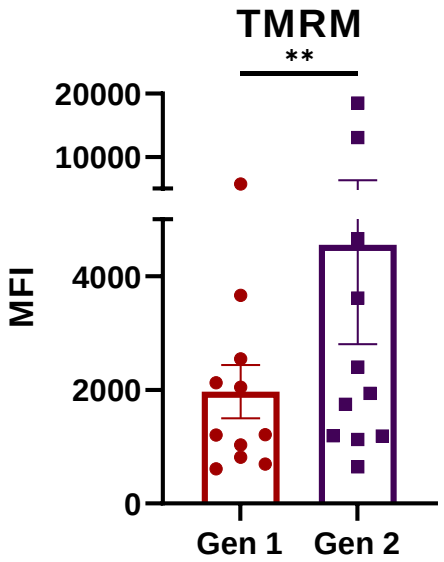


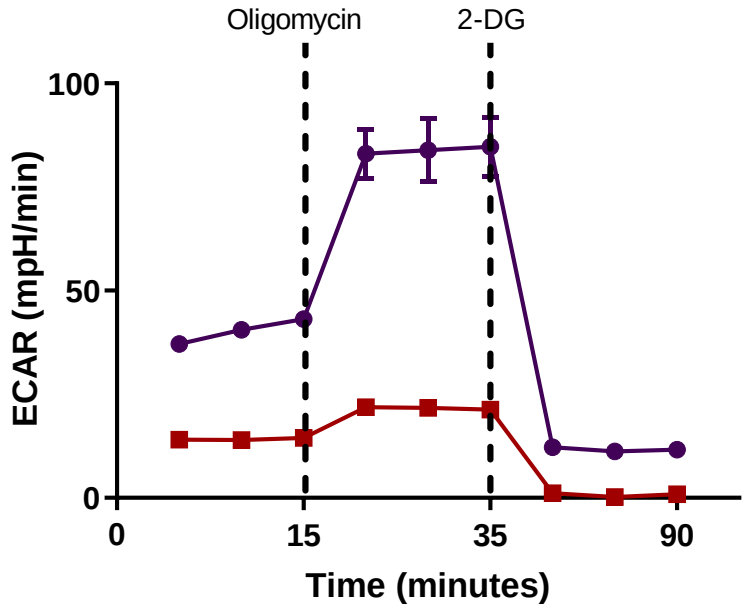
Improved metabolic fitness



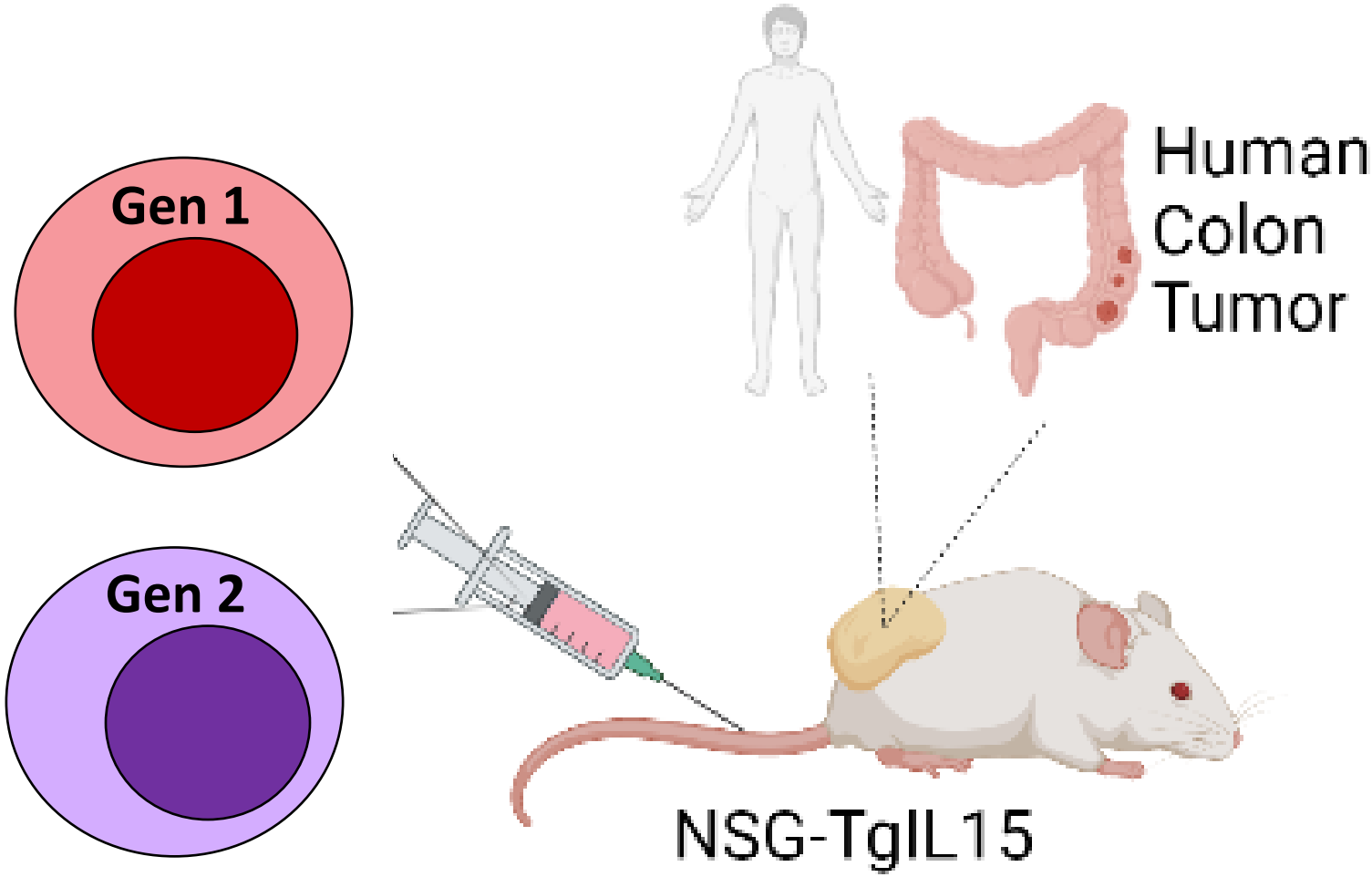




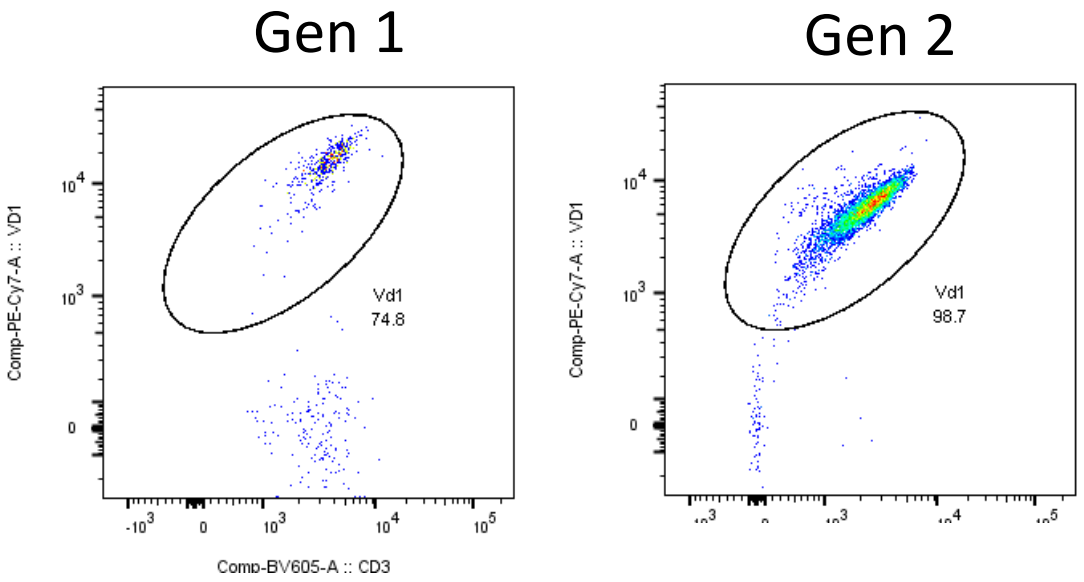


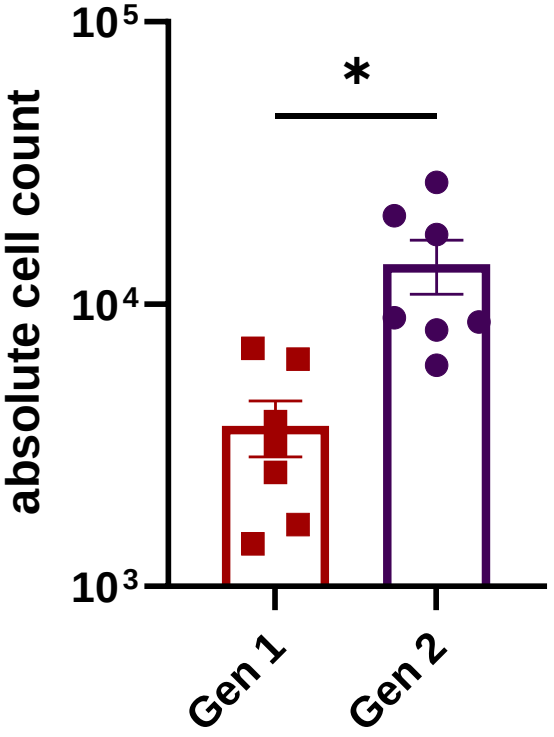


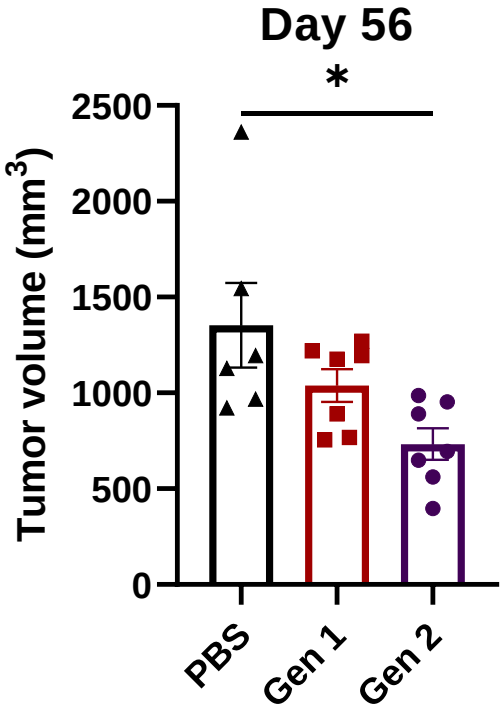
Gold standard test for both mitochondrial fitness and stability of phenotype is ***in vivo***

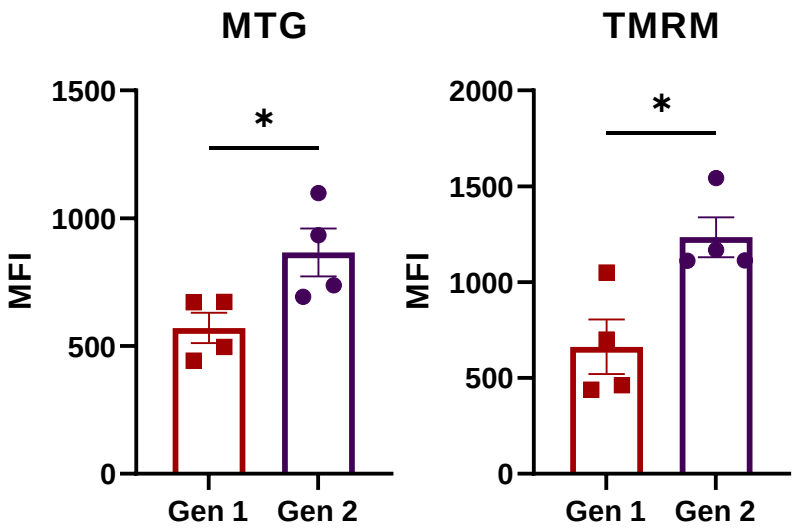


Gen 2 cells persist in tumor









Tumor 10,000 vs 120,000

Bone Marrow: 10,000 vs 900,000

iNKT cells are the Swiss Army Knife of the immune system

Cancer

Graft Versus Host Disease

Infection

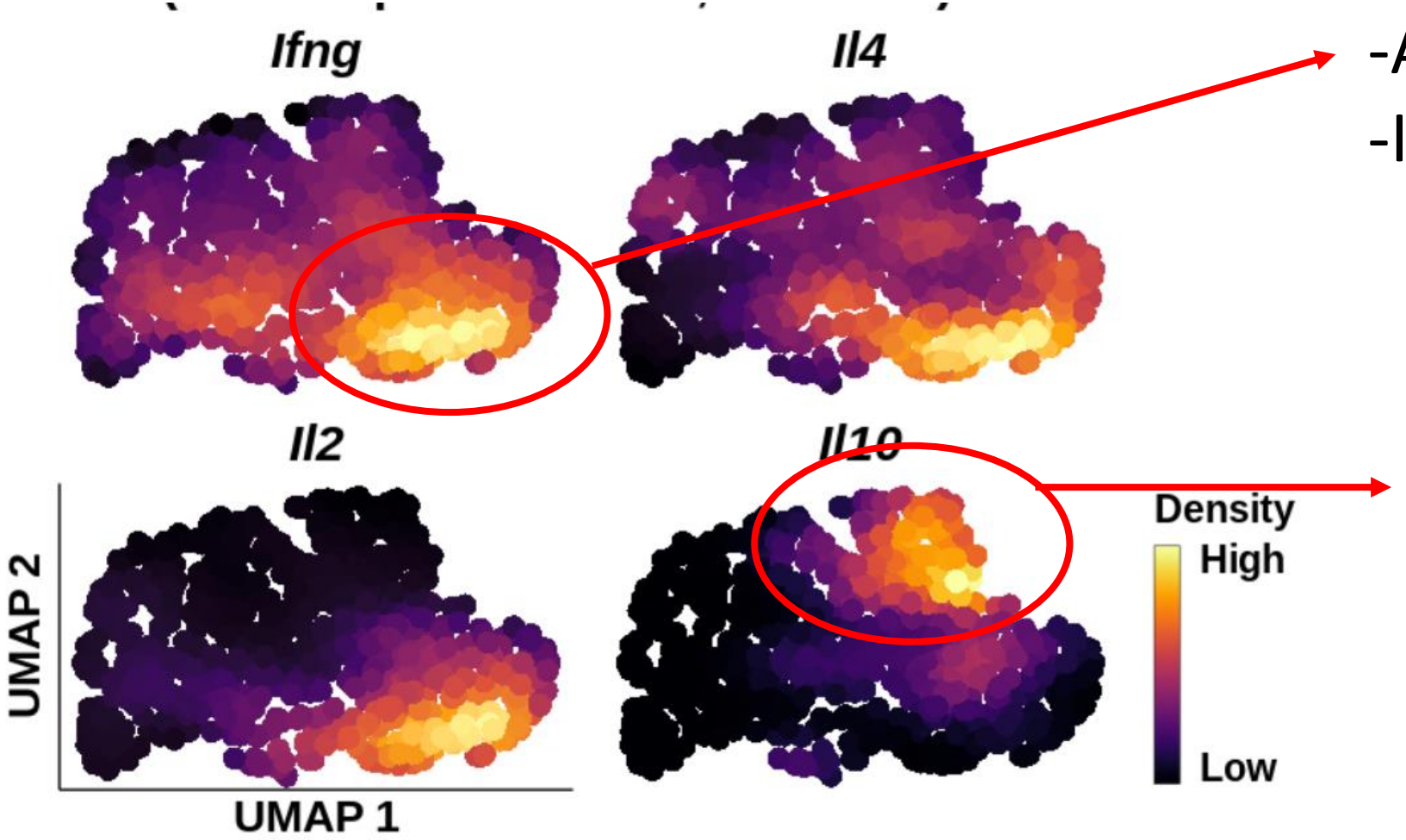
Requirement for checkpoint efficacy

Metabolism

- Type 2 Diabetes
- Reduction of inflammation associated with obesity

Weight and Energy Expenditure

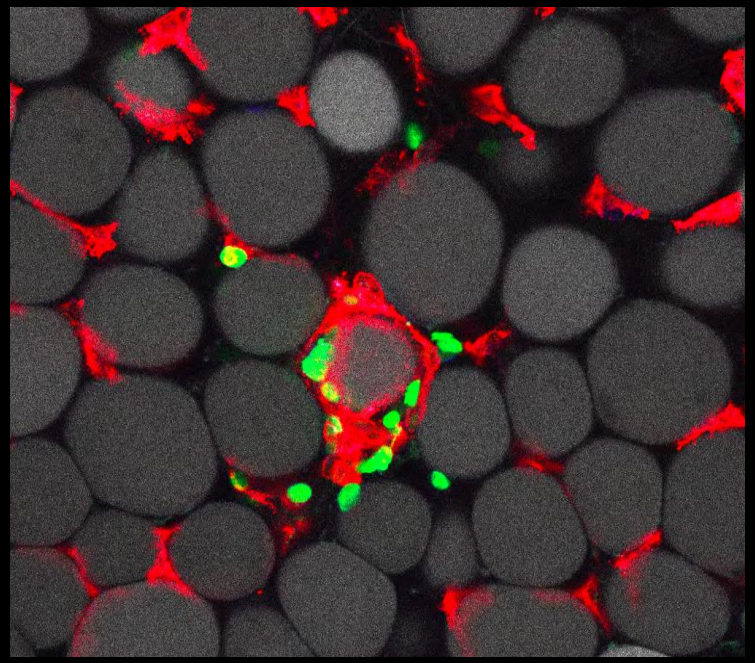
Harness transcriptional and metabolic programs associated with iNKT subsets for different conditions

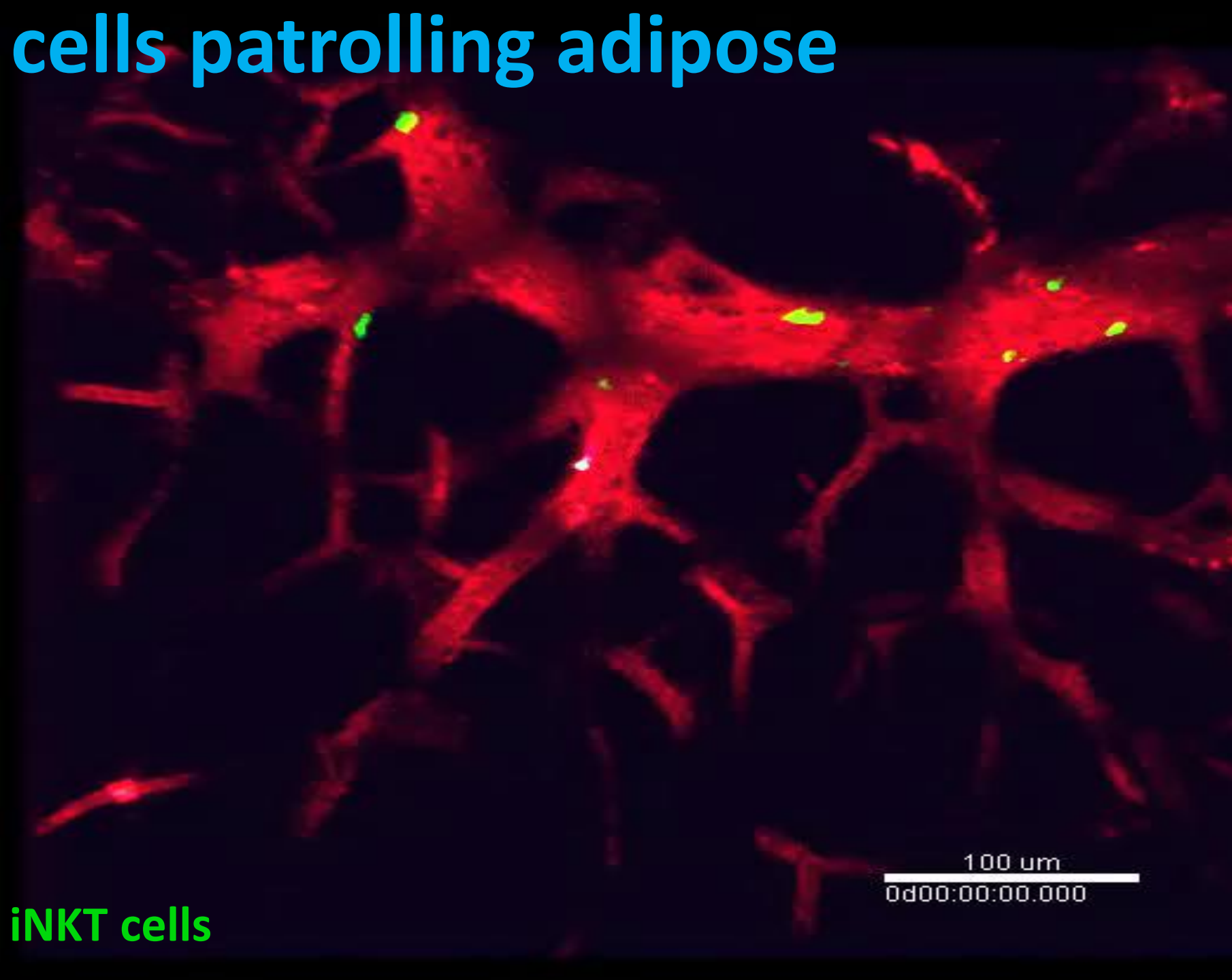


-Anti-tumor action
-Infection

-Anti-inflammatory
-Metabolic disorder
- GVHD

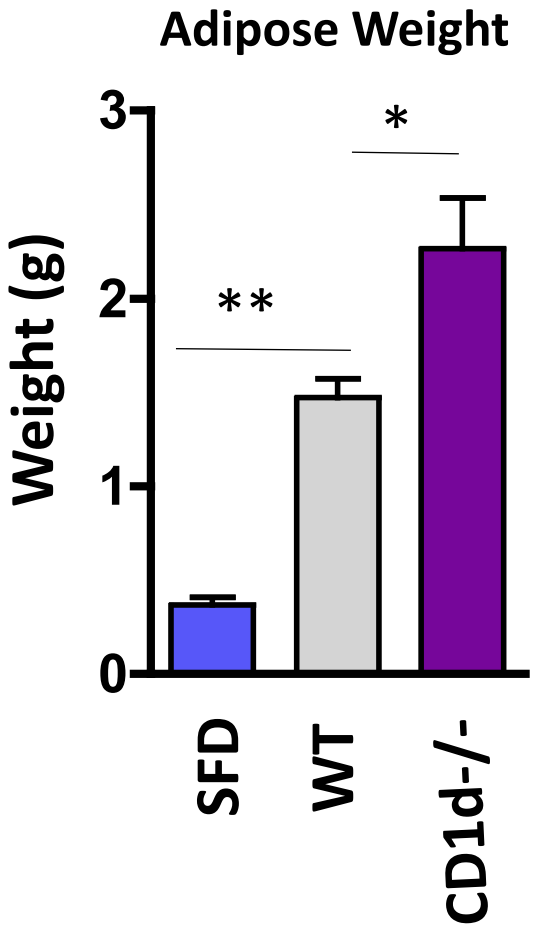
iNKT cells patrolling adipose

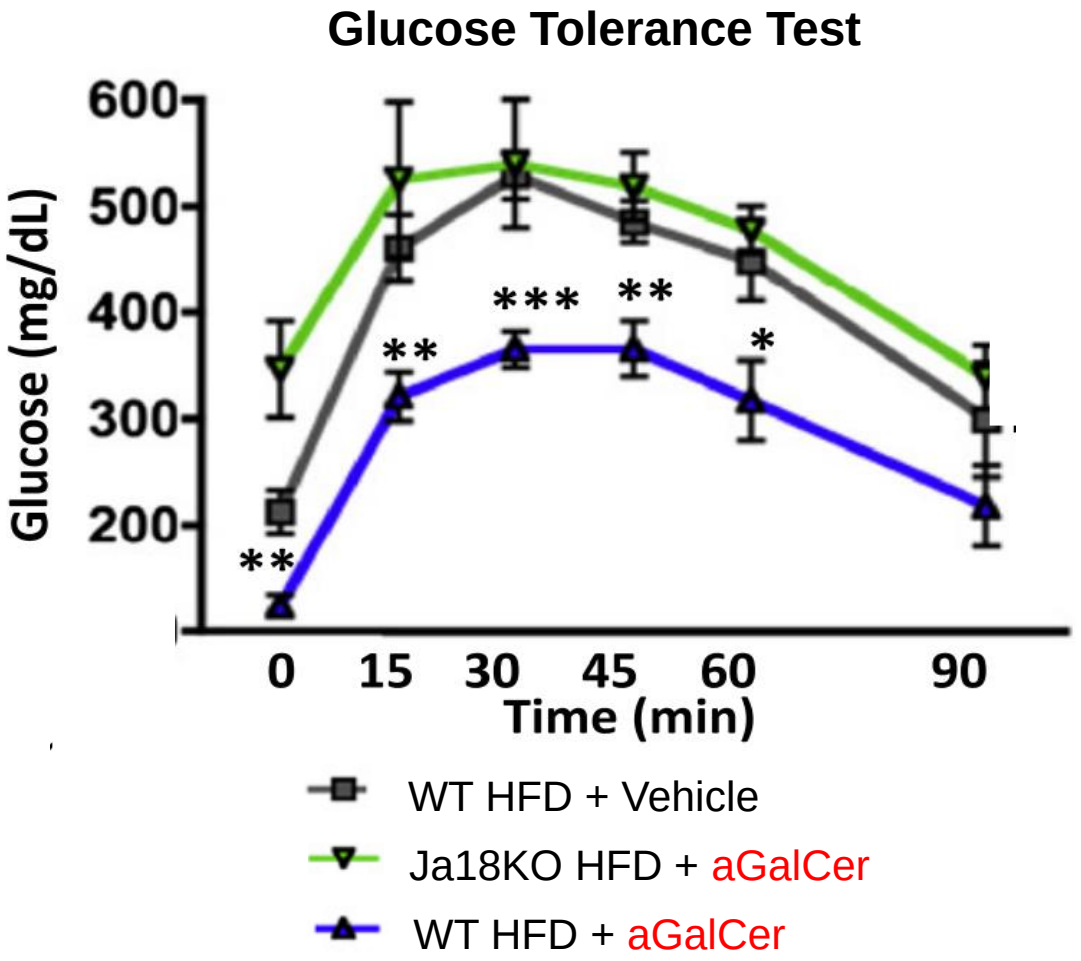


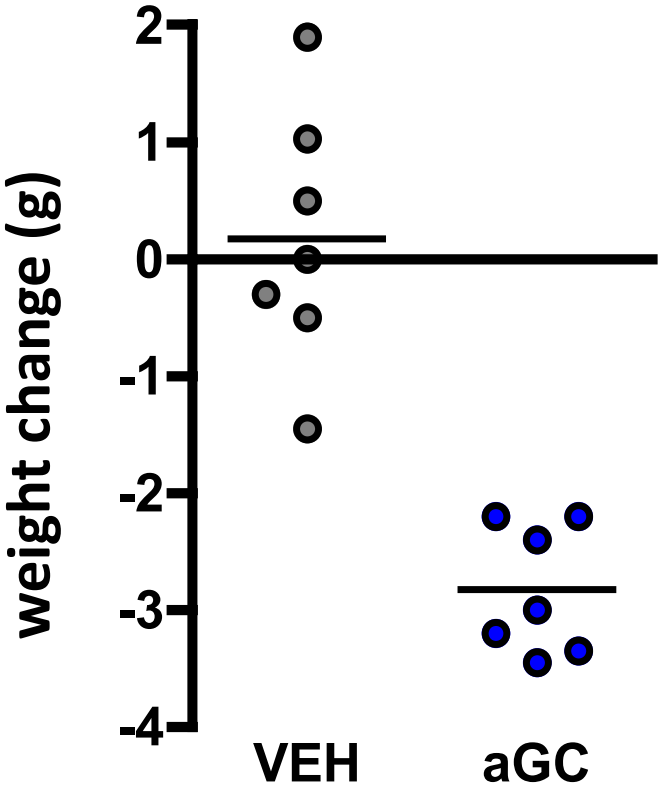


iNKT cells

Anti-inflammatory iNKT cells reverse metabolic disease in obesity







Lynch et al Nature Immunology 2015
Lynch et al Immunity 2012

Innate iNKT cells

- Versatile
- Transactivate of other cells
  – Conductor of the immune orchestra
- Can be expanded
- Can be manipulated for distinct functions

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R&D DAY

November 10th, 2022