Unleash Immunity

Corporate Presentation

May 2022

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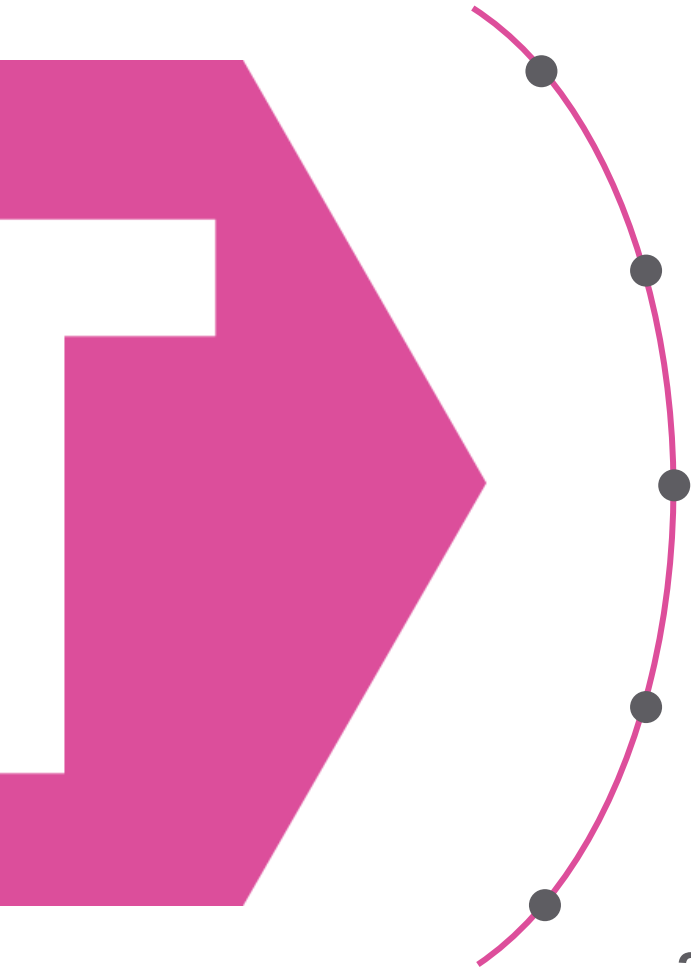
TScan highlights



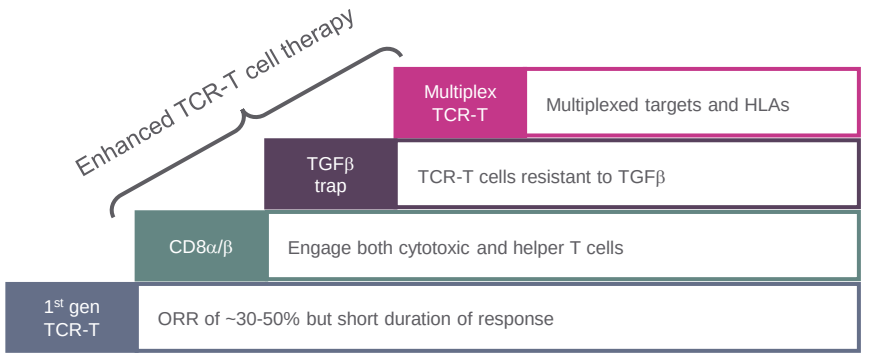
- Transformative Platform to Discover the Natural Targets of T cells
- Platform Enables Enhanced Multiplexed TCR-T cell Therapy
- Two INDs Filed in 2021; Additional INDs Planned for 2022
- Strategic Target Discovery Partnership with Novartis
- Cash Position of $140.8 MM as of 3/31/2022 Funds Company into 2024

TScan is differentiated from the competition by solving the three key challenges of TCR-T for solid tumors

1. TCR-T has shown high response rates, but limited durability

   TScan solution: *Enhance* TCR-T cells with CD8α/β and TGFβ trap

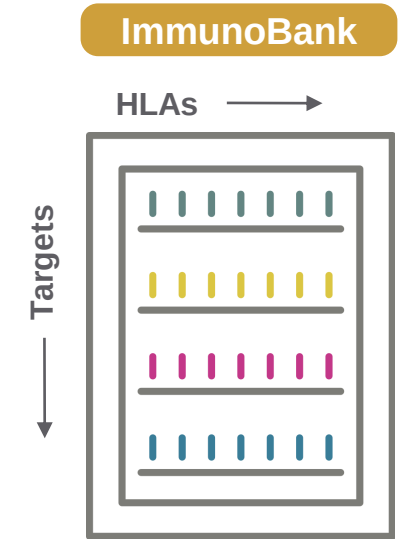
   TScan's manufacturing platform uniquely allows greater payloads



2. TCRs must be matched with the patient's HLA type

   TScan solution: *Expand* TCRs to include all common HLA types

   TScan's discovery platform uniquely enables rapid expansion of ImmunoBank



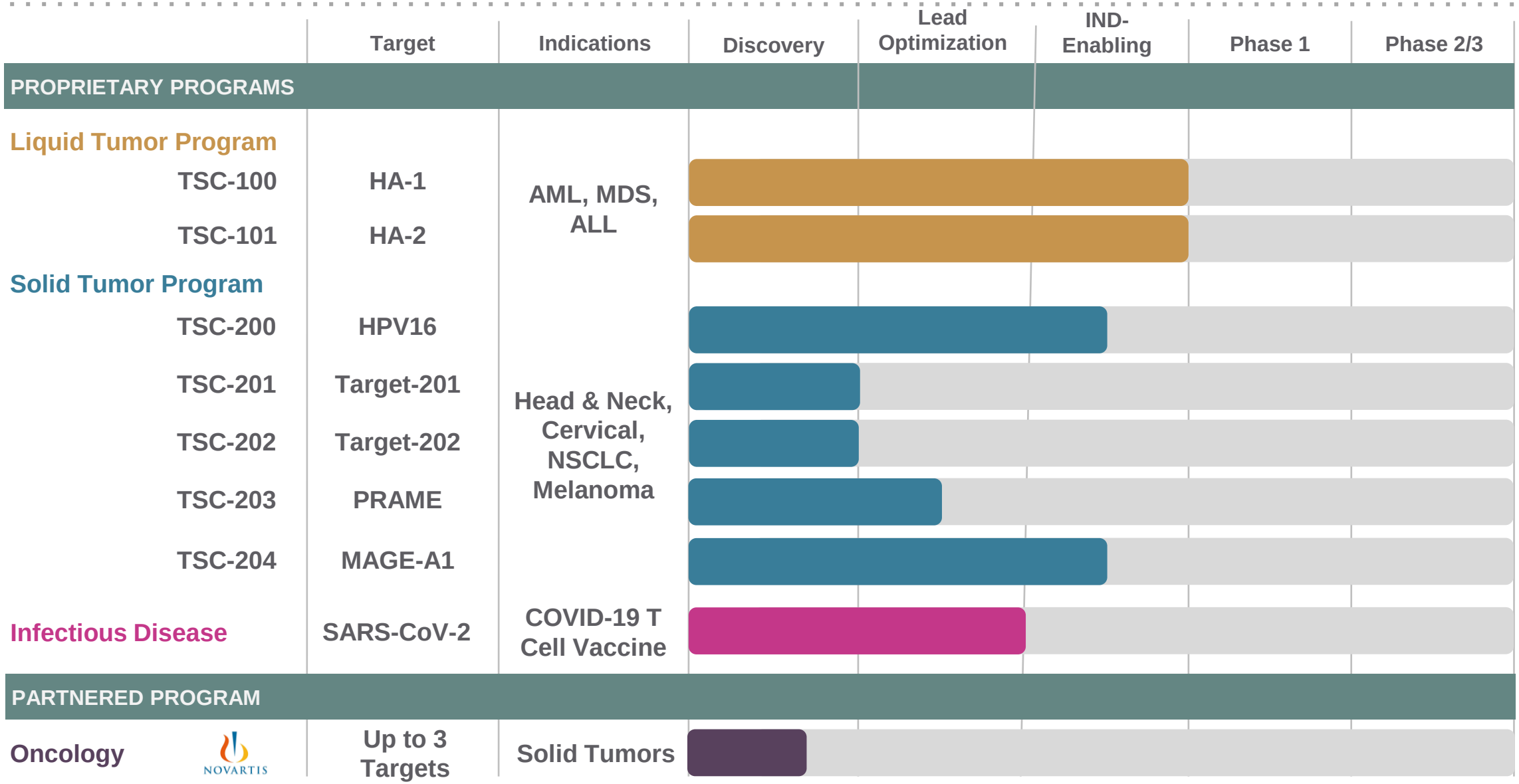
3. Solid tumors are heterogeneous (target expression and HLA loss)

   TScan solution: *Treat* patients with 2+ TCRs simultaneously

   Select patients based on HLA loss

   TScan is the only company actively pursuing multiplexed therapy

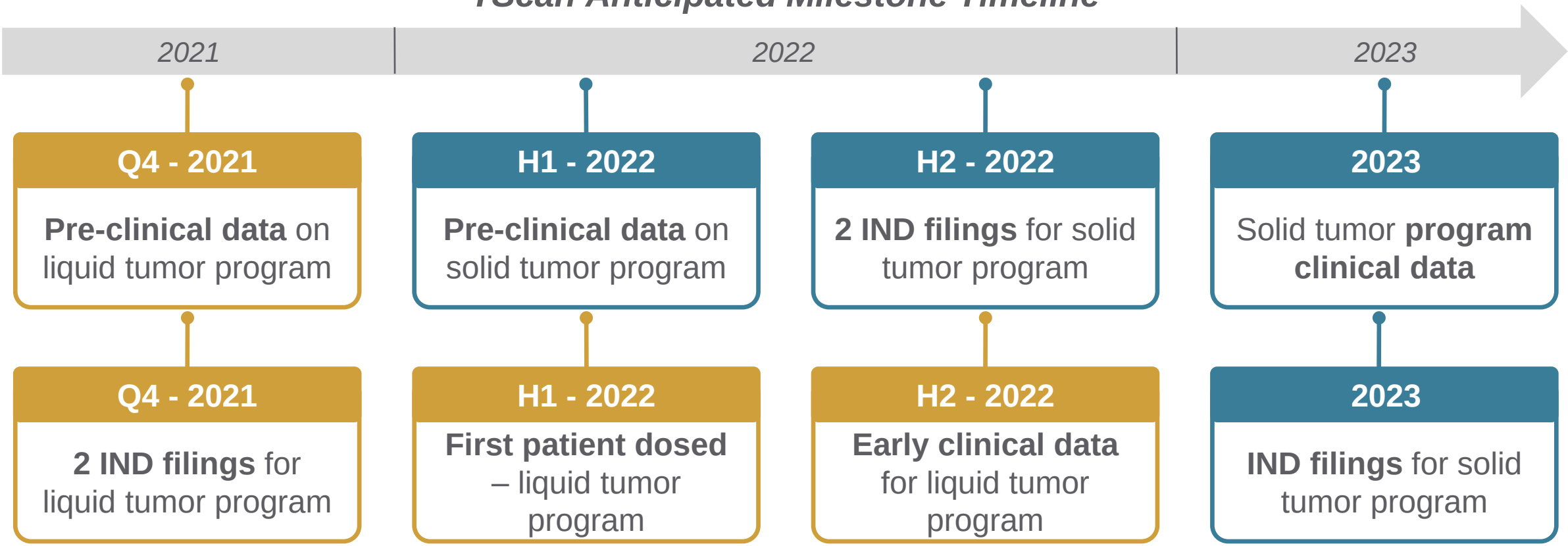
Platform delivers broad proprietary pipeline



TSCAN THERAPEUTICS

Broad pipeline drives multiple value-creating milestones

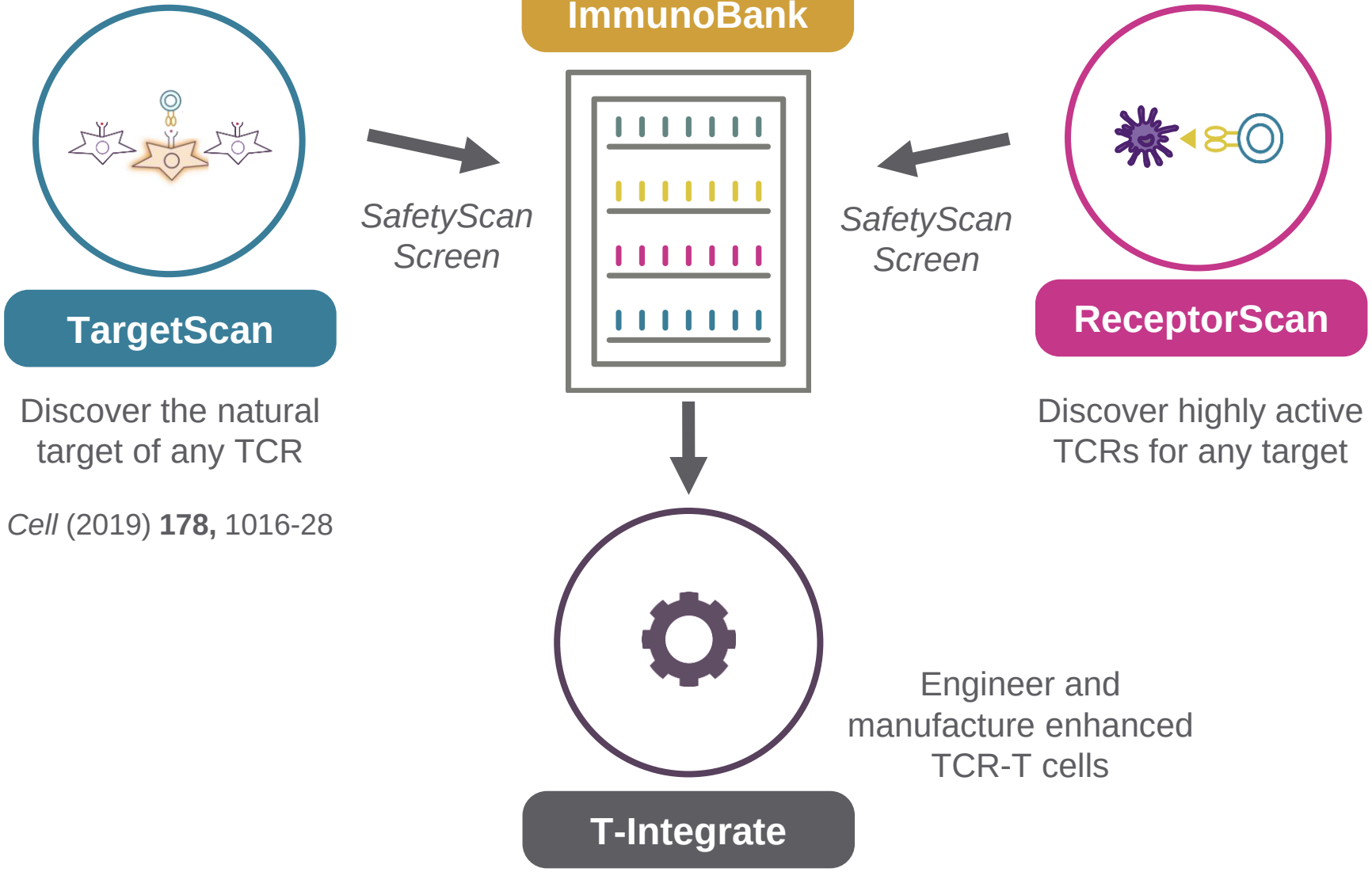
TScan Anticipated Milestone Timeline



Liquid Tumor Program | Solid Tumor Program

TScan Platform

Platform enables discovery and manufacturing of enhanced TCR-T candidates



Discover the natural target of any TCR

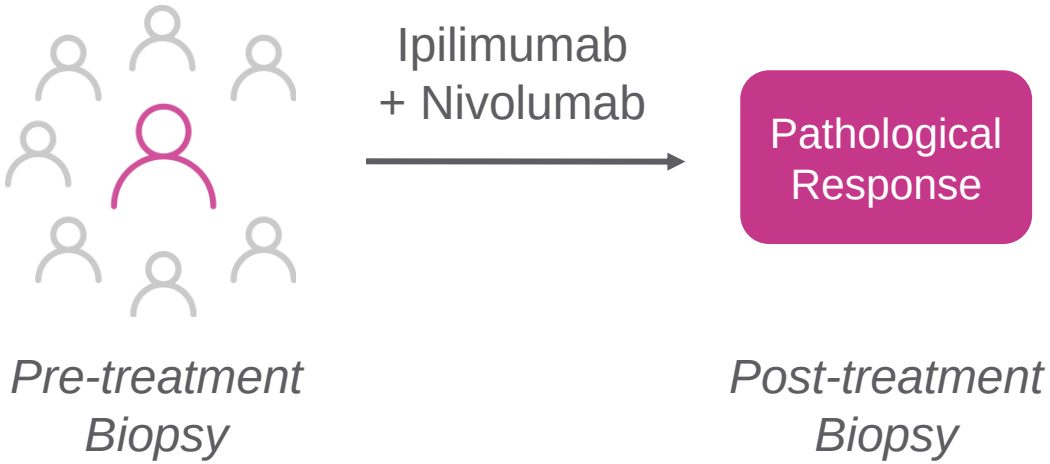
Cell (2019) **178,** 1016-28

Discover highly active TCRs for any target

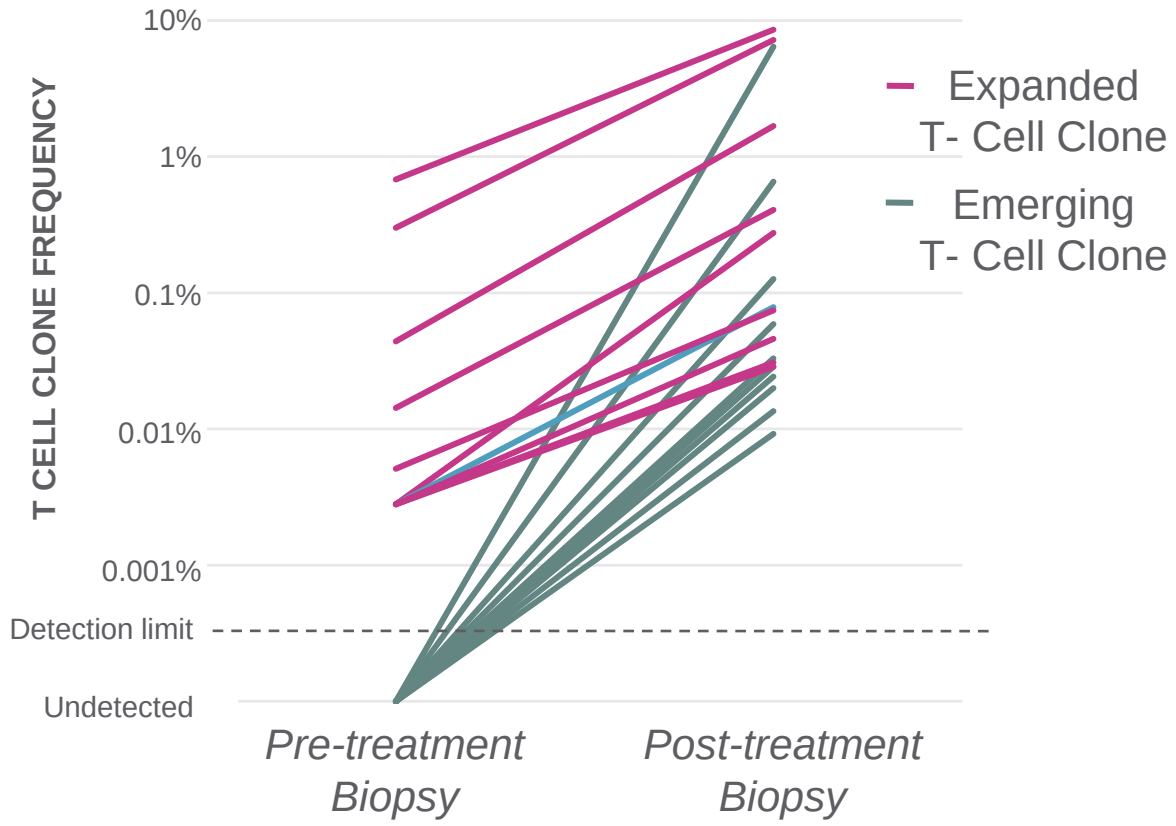
Engineer and manufacture enhanced TCR-T cells

Clinically active TCRs are identified from expanded T cells of Head & Neck cancer patients that respond to immunotherapy

Focus on patients that have exceptional responses to immunotherapy

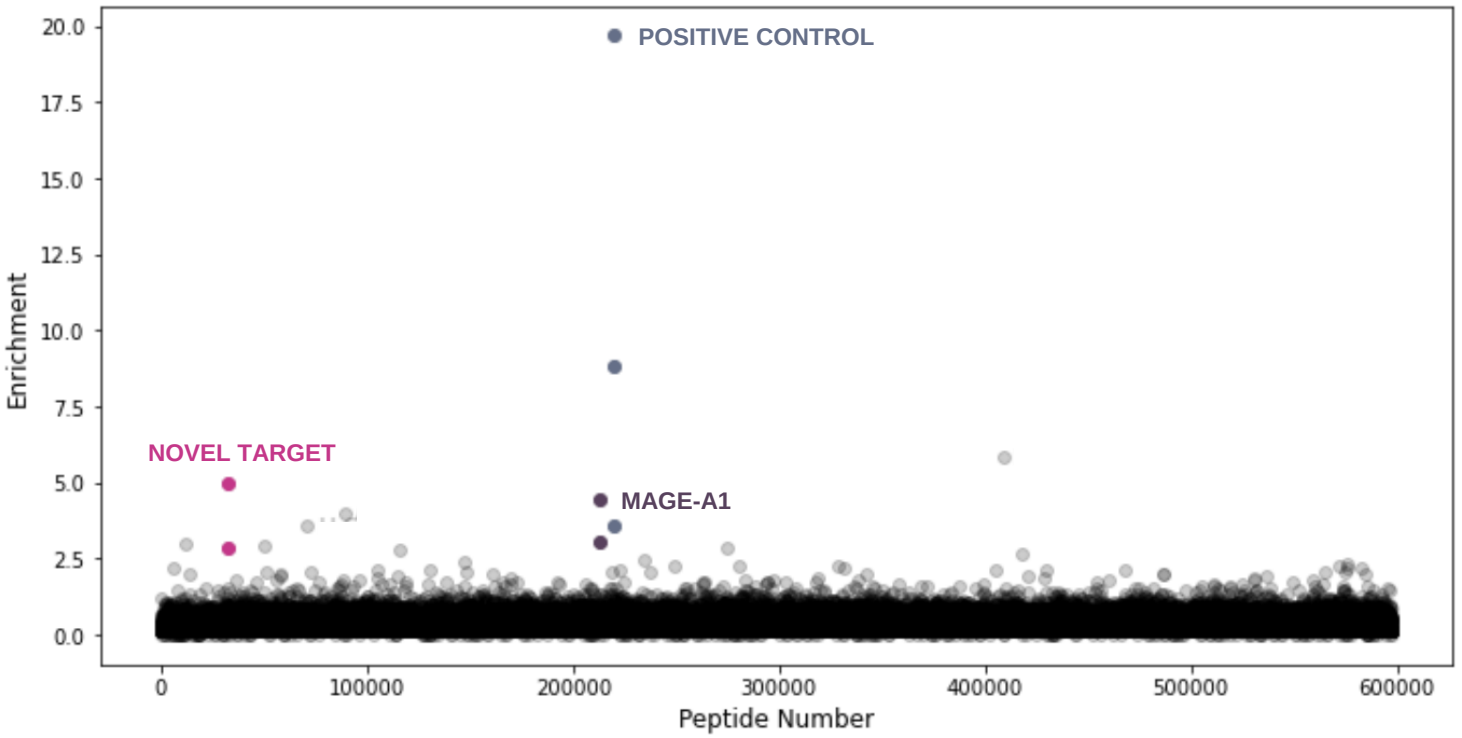


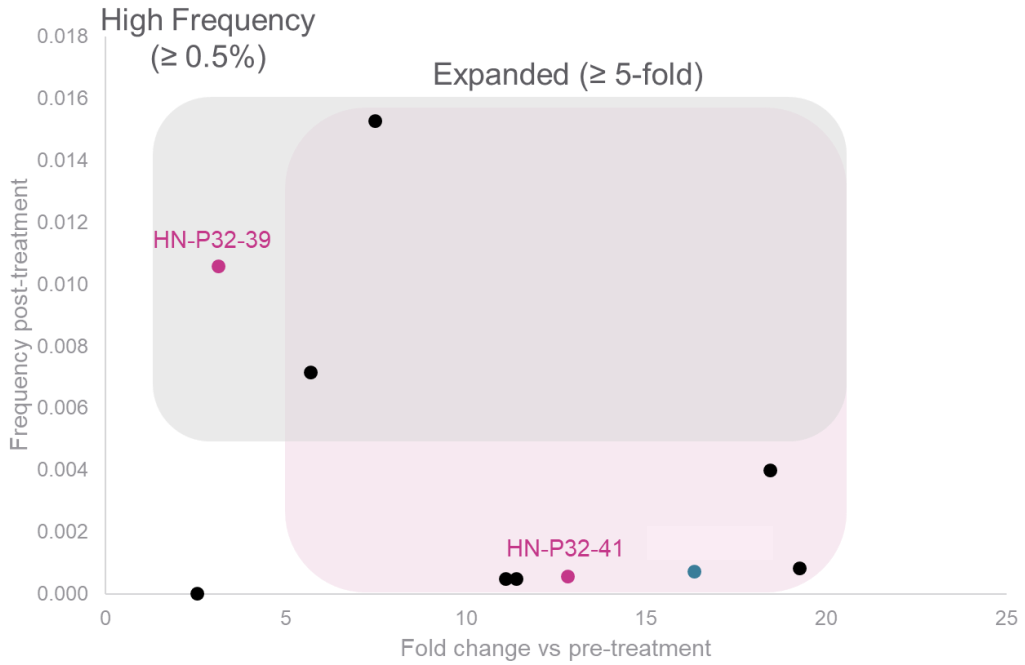
T cell sequencing data for a patient with a complete immunotherapy response



Multiplexed screen identified MAGE-A1 as a target in a Head & Neck cancer patient responding to immunotherapy

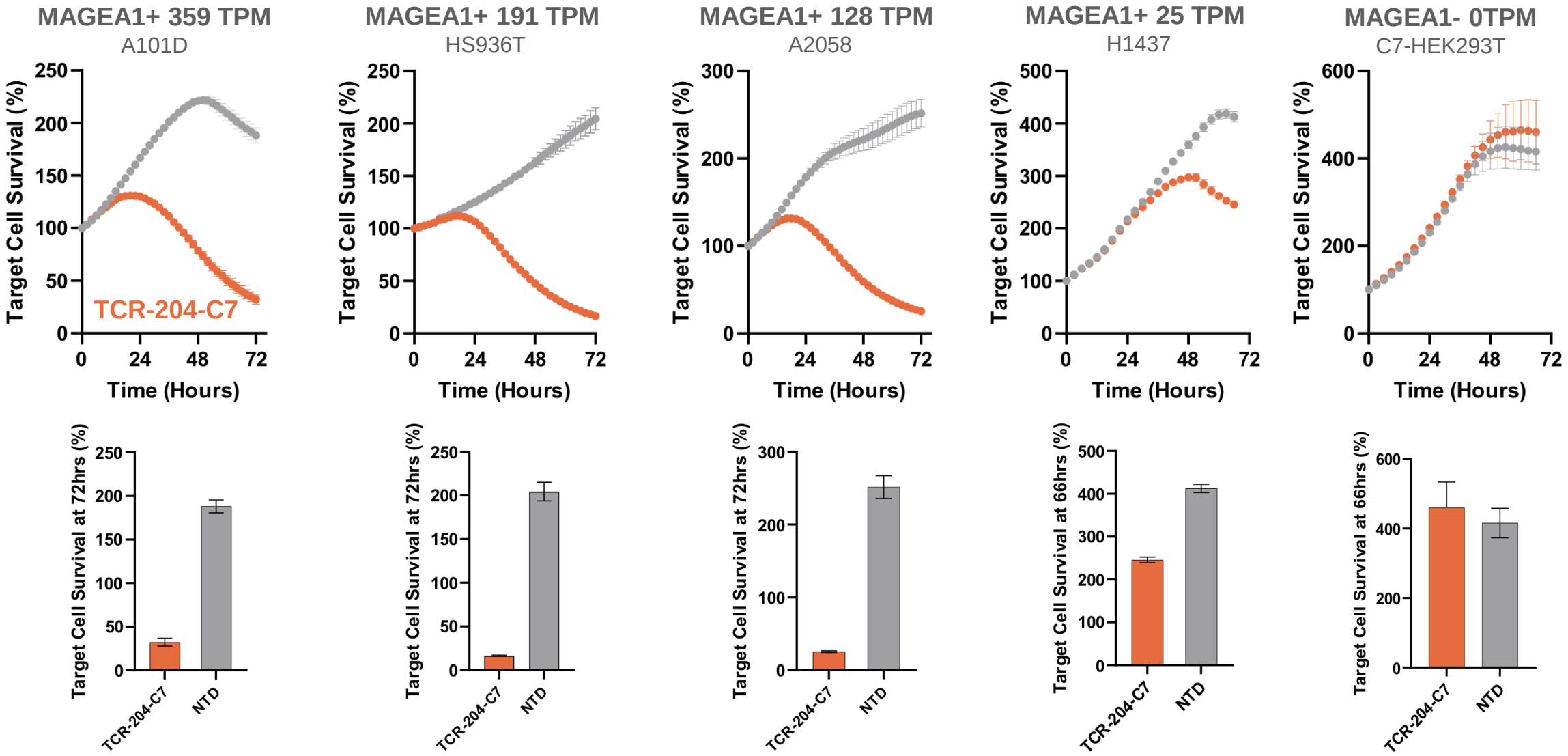
- Patient 32 had 60% reduction in primary tumor size following anti-PD1 and anti-CTLA4 therapy





TCR	Target	HLA
HN-P32-39	MAGEA1	C*07:02
HN-P32-41		

TScan's TCR-204-C7 shows strong in vitro activity



ReceptorScan identifies ultrahigh affinity, naturally occurring TCRs with low risk of off-target effects

Key Problem

CHALLENGE

Most naturally-occurring TCRs to self antigens have low affinity and/or low activity

CURRENT SOLUTIONS

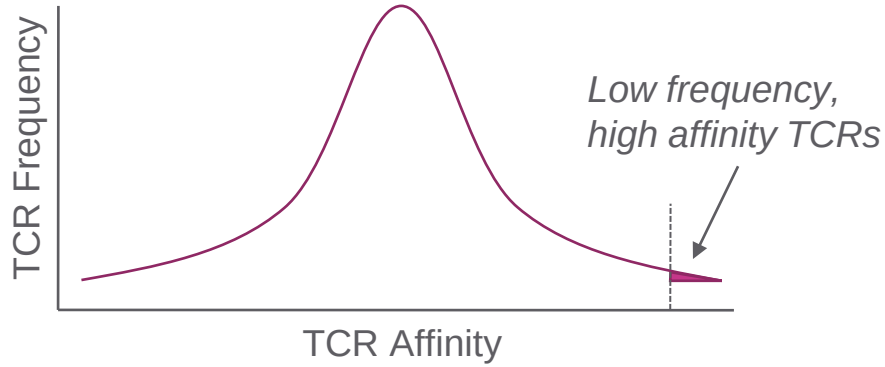
- Mutate TCRs to enhance affinity
- Raise TCRs in transgenic mice

PROBLEM WITH THESE SOLUTIONS

TCRs that have not undergone negative selection in the thymus may exhibit off-target effects

TScan Solution

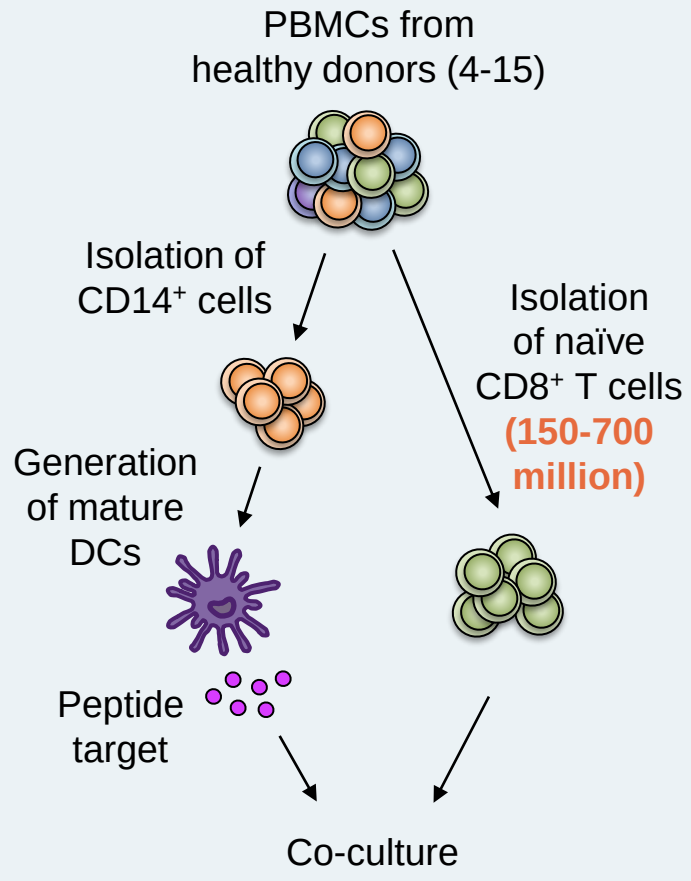
ReceptorScan is a high-throughput platform that identifies the best TCR for a desired target from >1 billion T cells



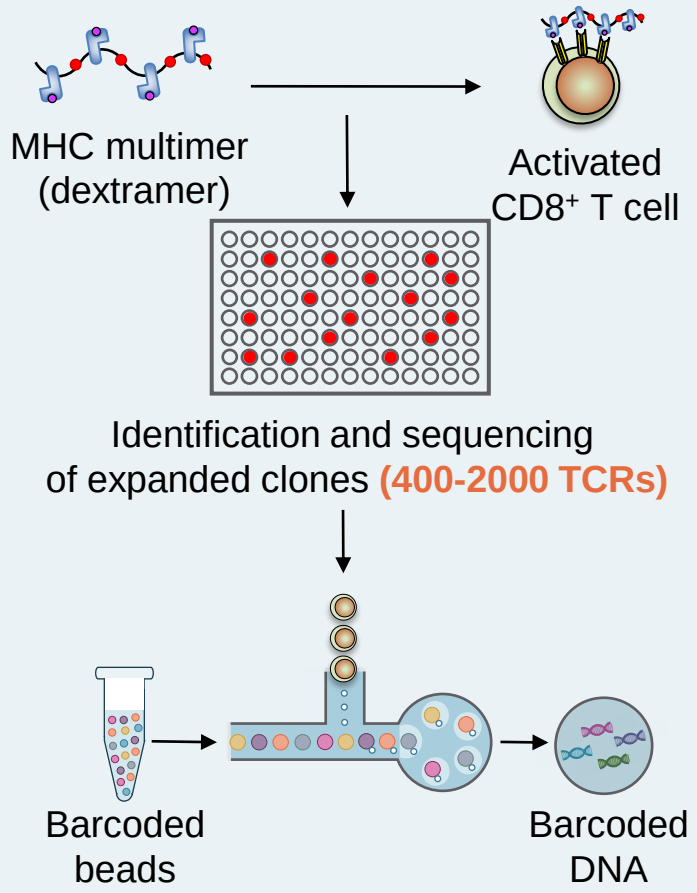
All TCRs are fully human and naturally occurring, yet exhibit affinities equal to or better than clinical-stage TCRs

ReceptorScan platform identifies natural high-affinity TCRs for identified targets and desired HLA restrictions

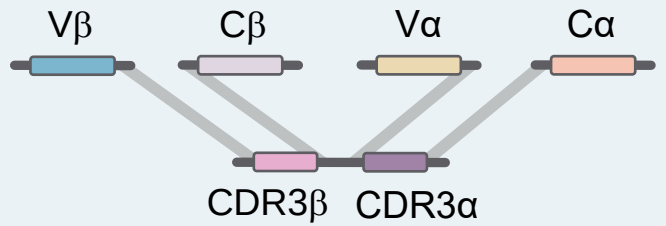
1 Expansion of target-specific CD8⁺ T cells



2 Isolation and single-cell sequencing of CD8⁺ T cells

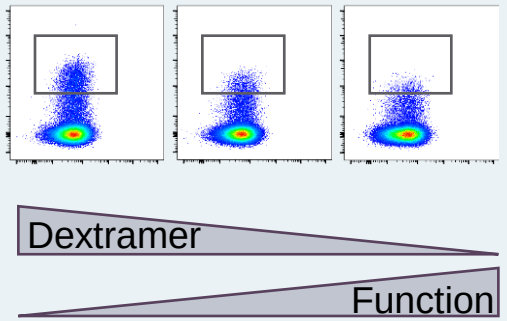


3 Gene synthesis and cloning of TCR libraries



PISTACHIO cloning

4 Selection of rare TCRs with ultra high affinity & activity



Enrichment of superior TCRs

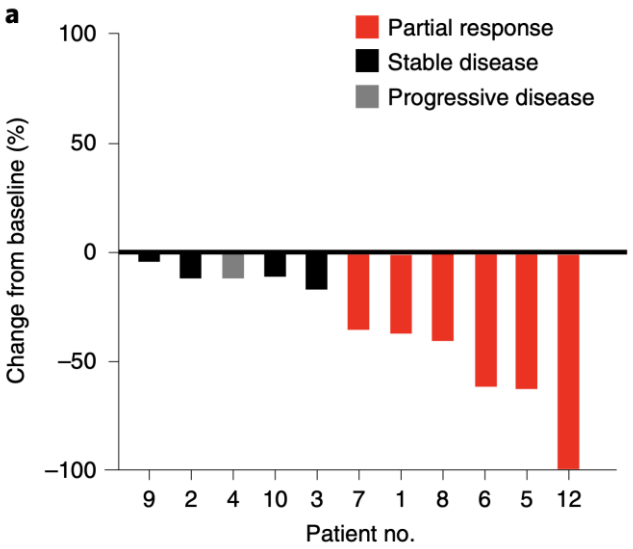
(10-50 lead TCRs)

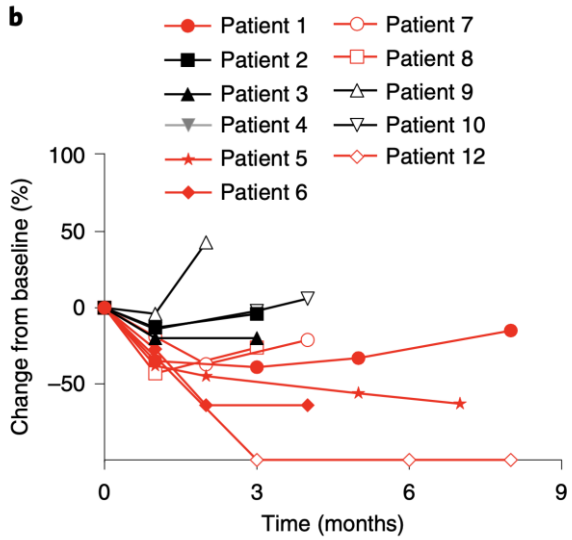
The most dramatic TCR-T results to date in solid tumors were achieved by targeting E7 of HPV

nature medicine
LETTERS
https://doi.org/10.1038/s41591-020-01225-1
Check for updates

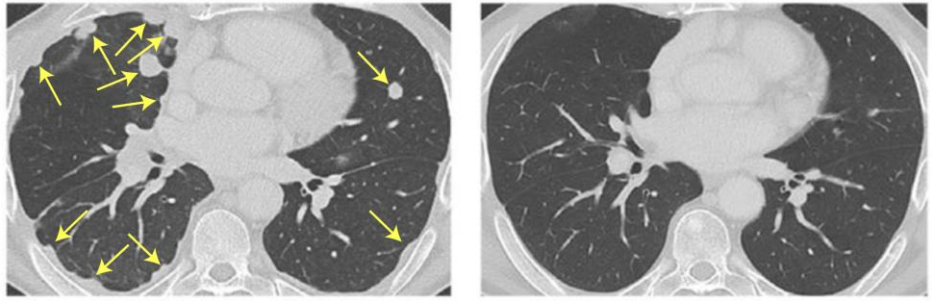
TCR-engineered T cells targeting E7 for patients with metastatic HPV-associated epithelial cancers

Nagarsheth NB, …, Hinrichs CS (2021) *Nature Medicine,* **27**, 419-425.





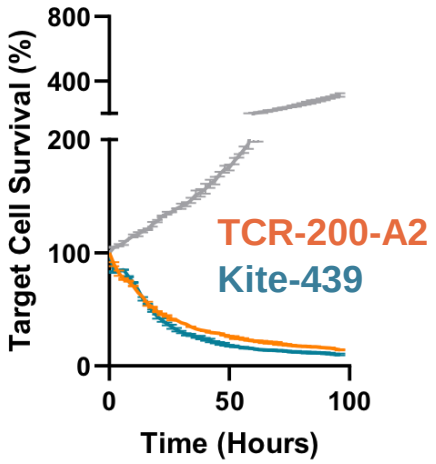
Before treatment **7 months**

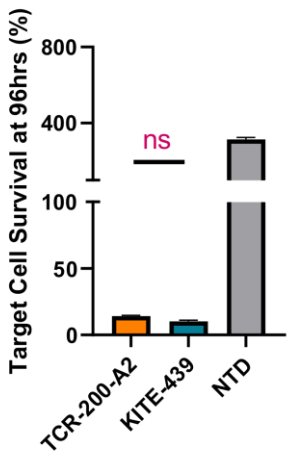


"Patient 5 had metastatic anal SCC with more than 90 metastatic tumors that involved the thorax, retroperitoneum, bones and kidney. He had been treated previously with chemoradiation and with PD-1-based therapy. He experienced a nine-month partial response with complete regression of ~80 tumors that remained absent from imaging 14 months after treatment."

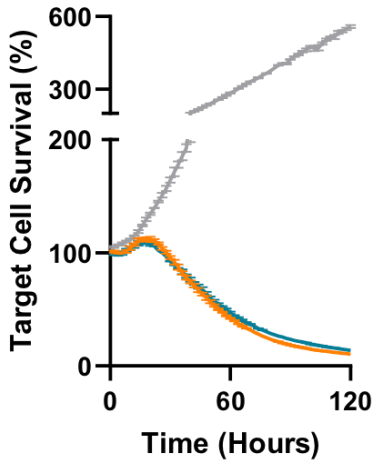
TScan's TCR-200-A2 shows comparable activity to Kite-439

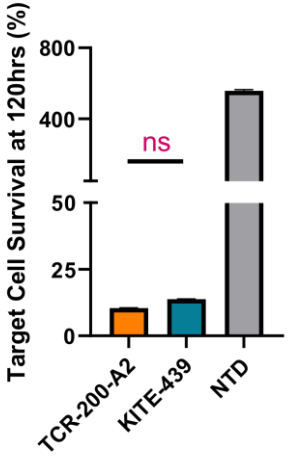
HLA-A*02:01+ HPV16+
CaSki



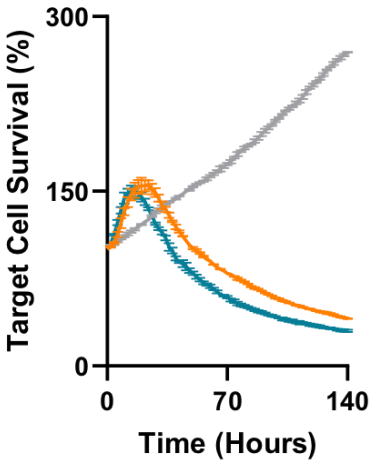


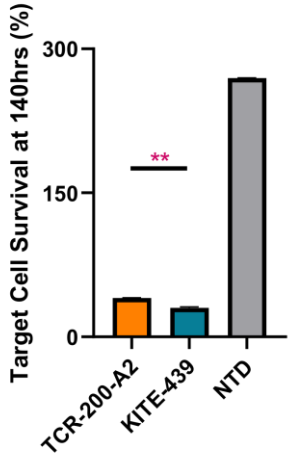
HLA-A*02:01+ HPV16+
SCC152



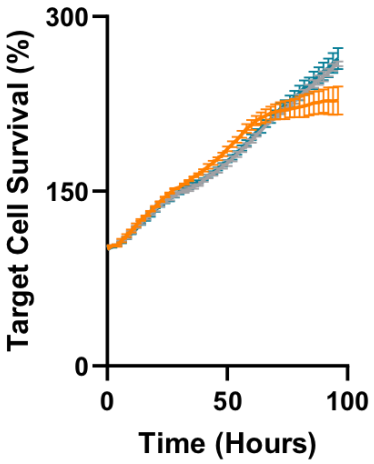


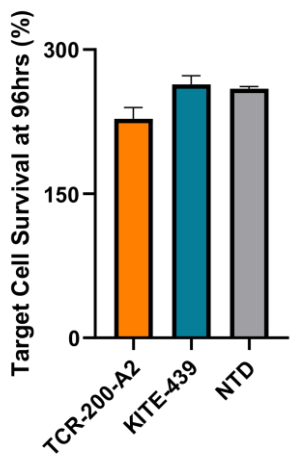
HLA-A*02:01+ HPV16+
SCC090



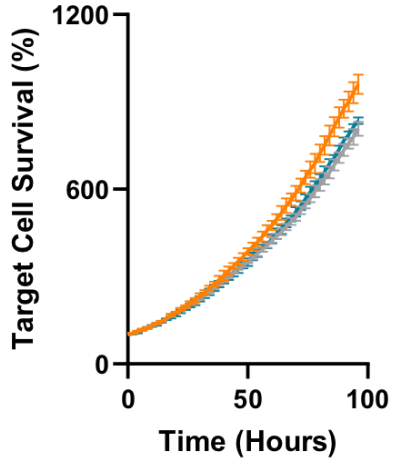


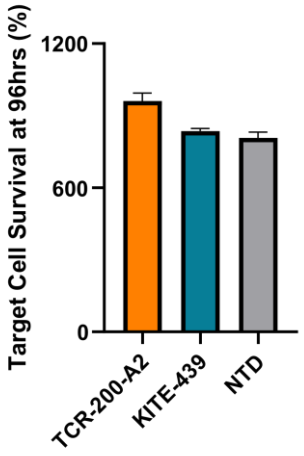
HLA-A*02:01- HPV16+
SiHa





HLA-A*02:01+ HPV16-
NCI-H1792



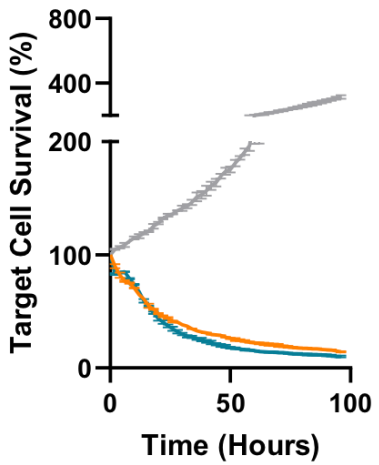


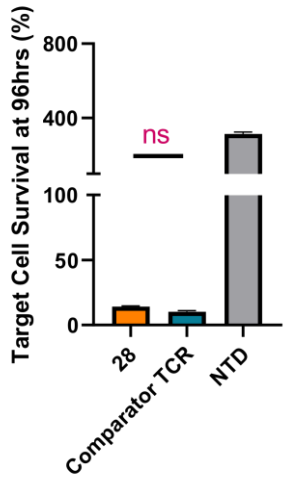
* Calculated with one way ANOVA, Dunnett's multiple comparisons test

TScan's TSC-200-A2 shows superior effector function to comparator NCI TCR

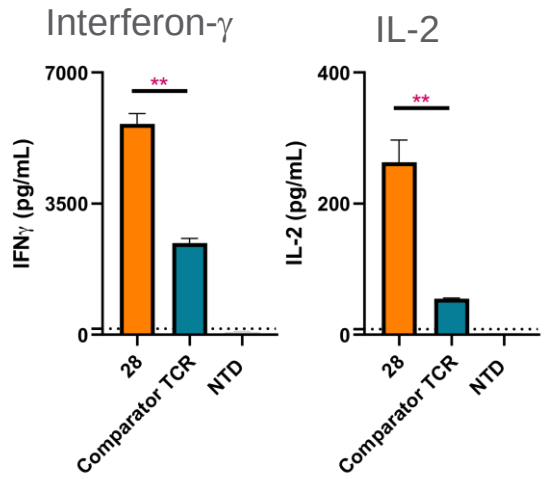
CaSki (HLA-A*02:01+ HPV16+)

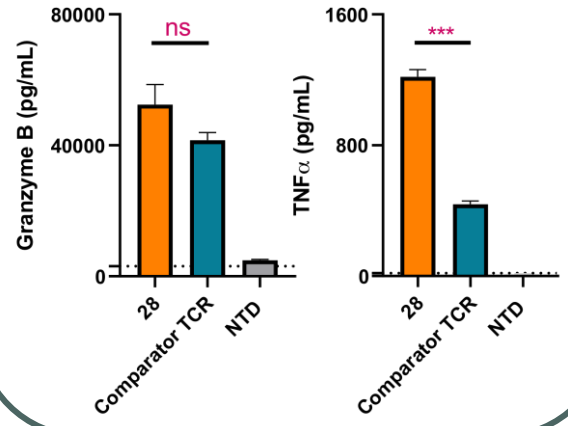
Cytotoxicity



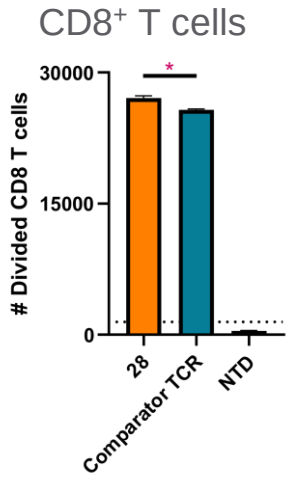


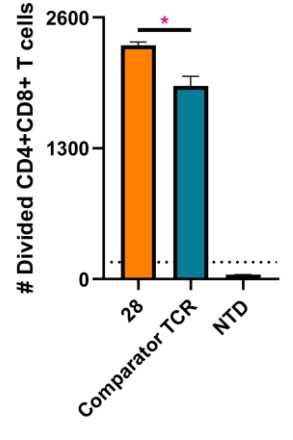
Cytokine production





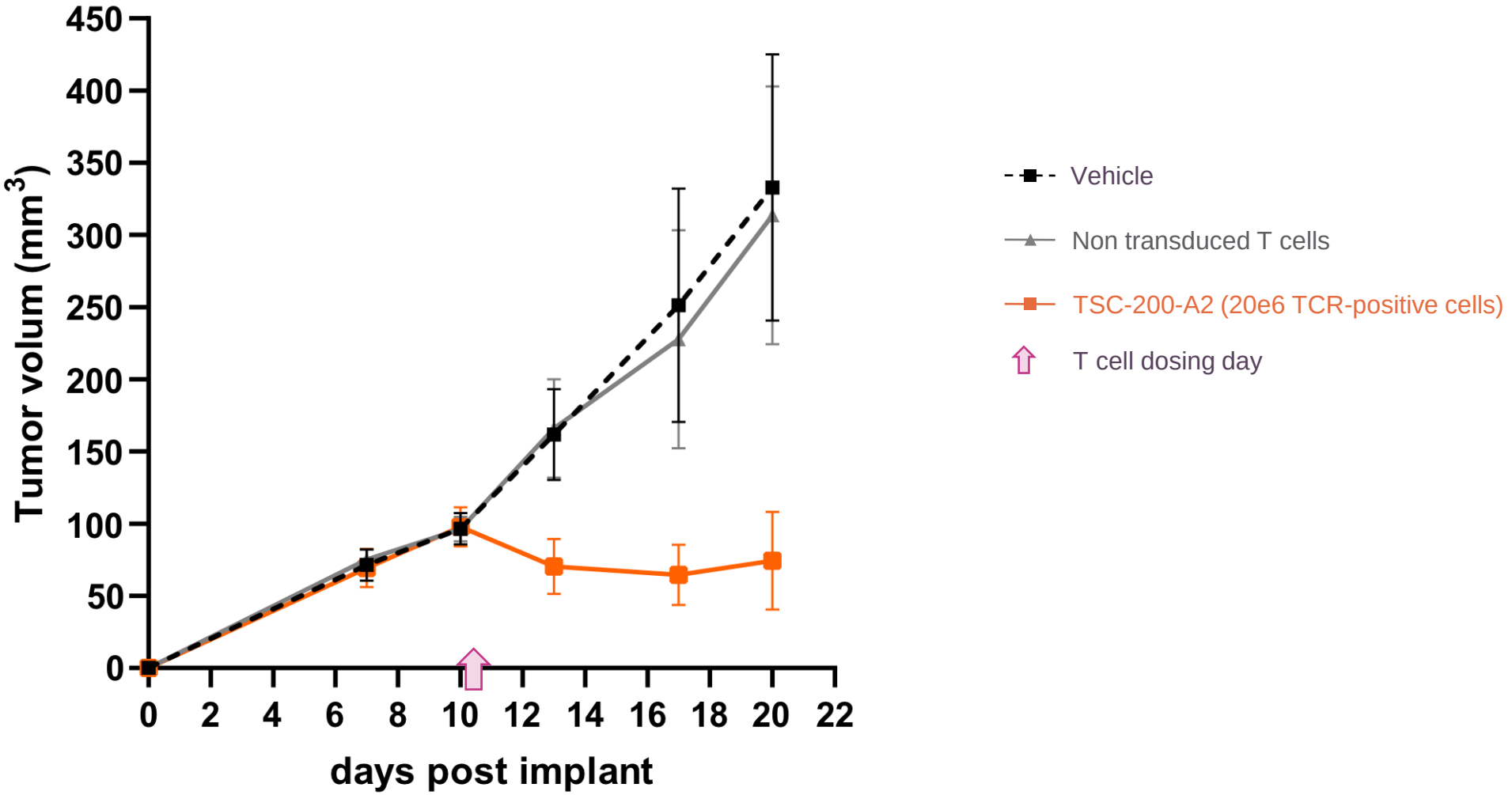
T cell proliferation



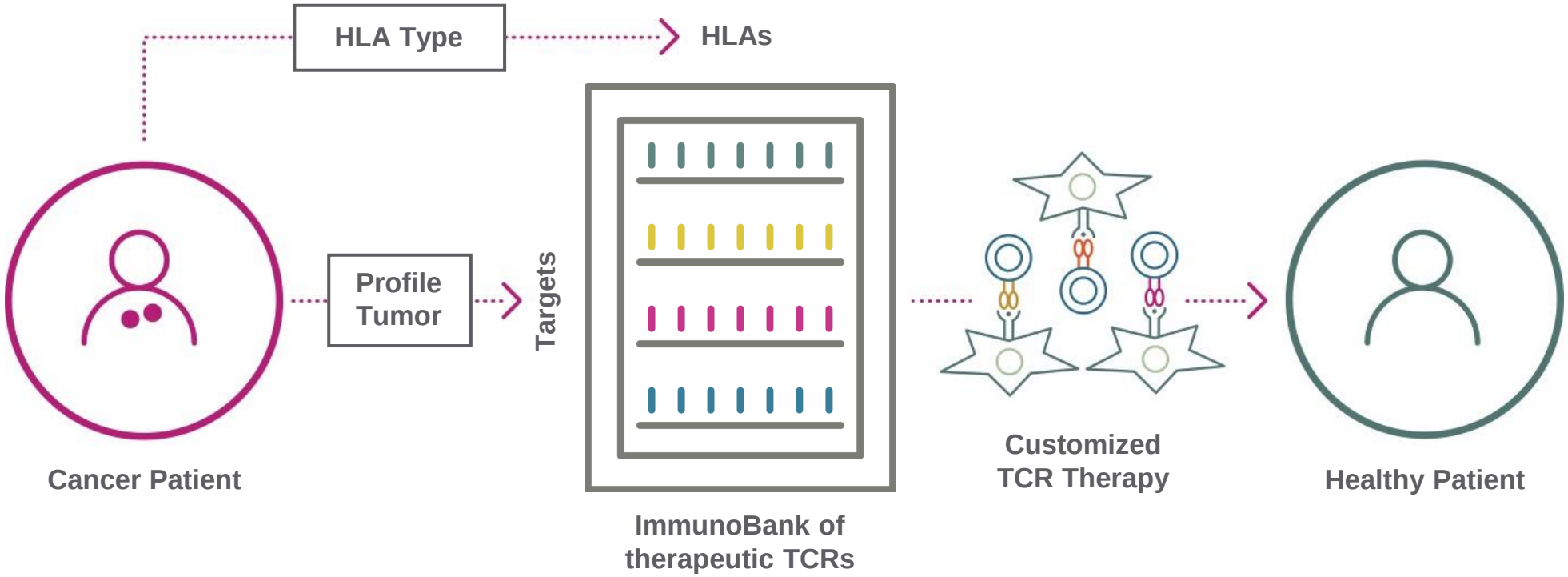


* Calculated with one way ANOVA, Dunnett's multiple comparisons test

TSC-200-A2 shows promising activity in a mouse model of HPV-positive cancer



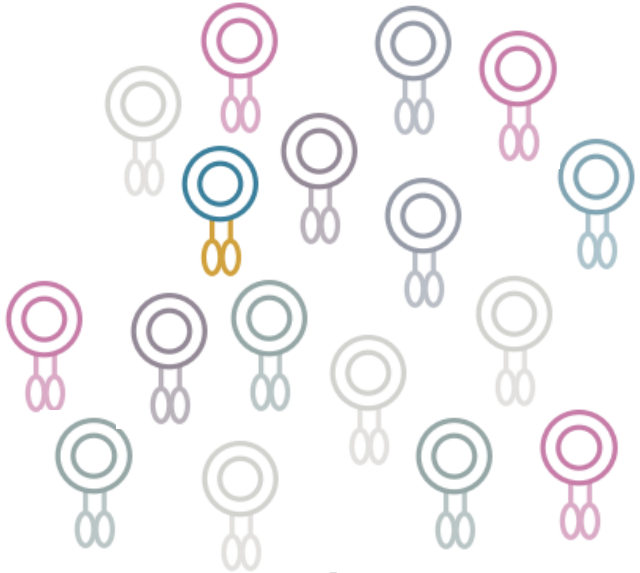
Vision is to build a diverse ImmunoBank of TCRs to provide customized, off-the-shelf, multiplexed TCR-T



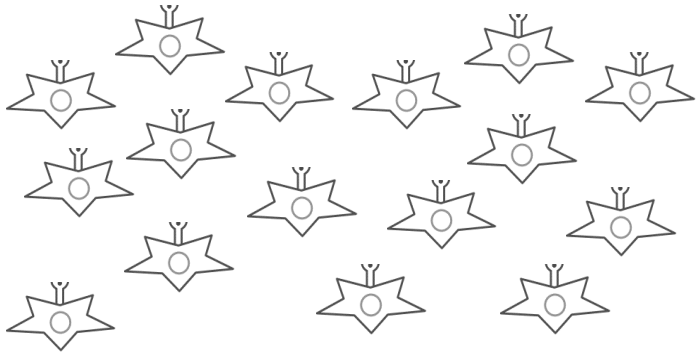
Multiplexed TCR-T may overcome both **tumor heterogeneity** and resistance due to **HLA loss**

T-Fish enables directed target discovery of patient-derived T cells that recognize a particular target of interest

Pool of T cells from a cancer patient



HEK cells expressing **HLAs** and **target of interest**



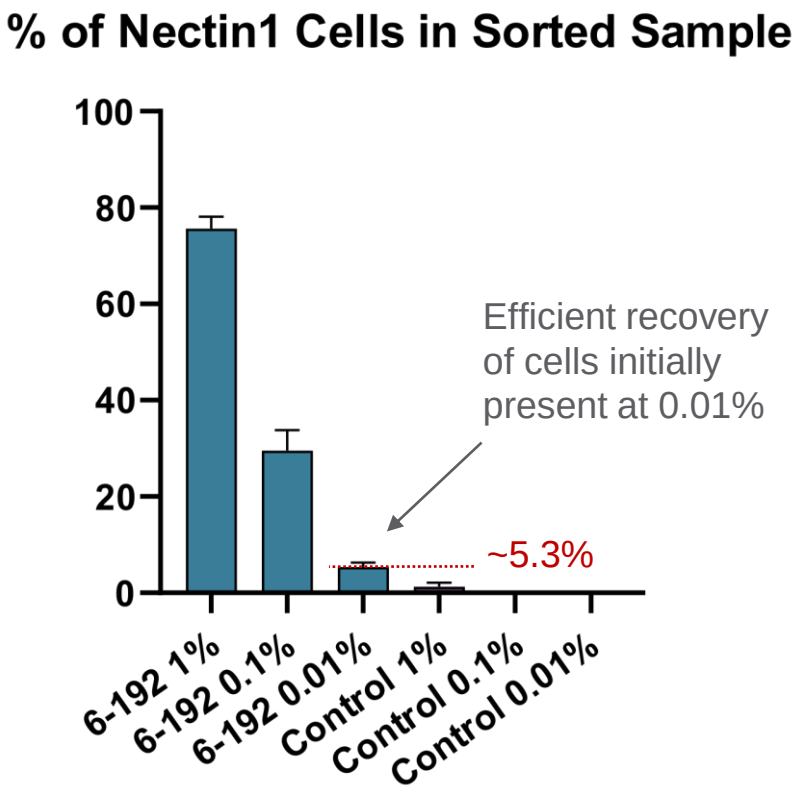
AIM+ MACS → AIM+ FACS

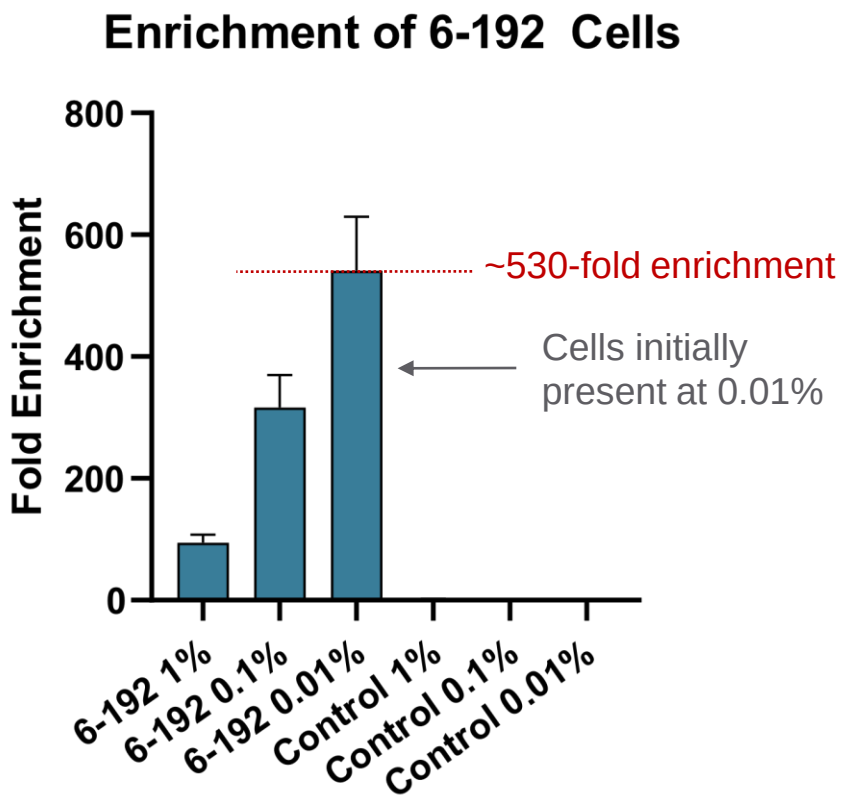
Target-reactive T cell for new HLA type

Targets include oncogenic viruses, C/TAs, etc.

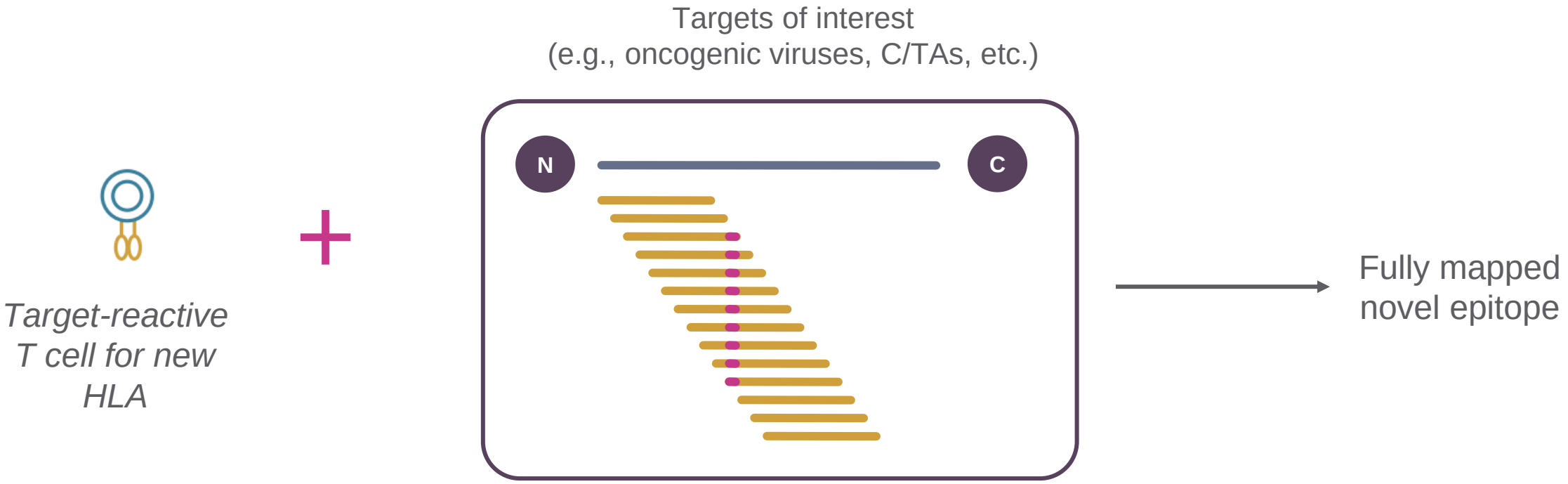
T-Fish can identify T cells present at 1 part in 10,000

- Proof-of-concept conducted with T cells that recognize Nectin1
- Nectin1-reactive T cells (6-192) spiked in at varying percentages





EpitopeScan enables rapid identification of the precise epitope of target-reactive T cells



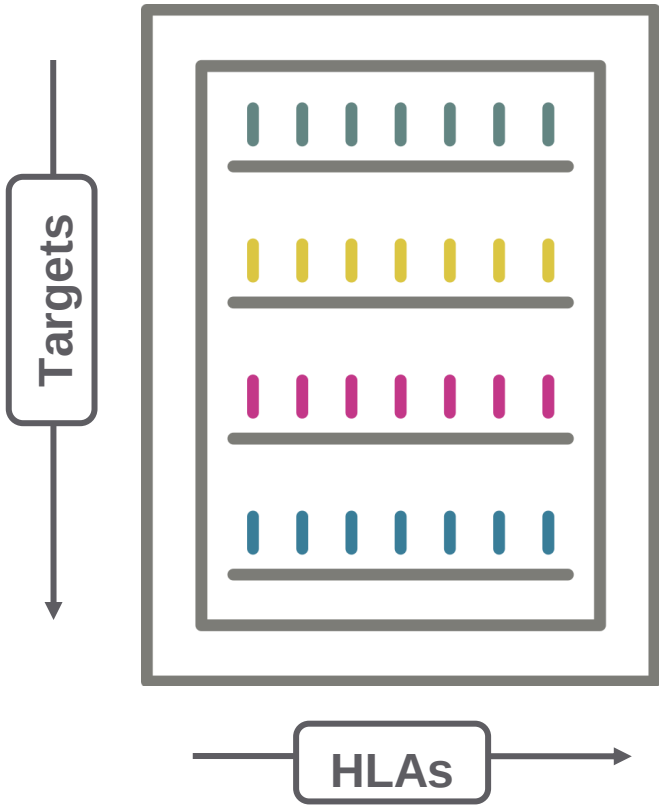
Current EpitopeScan library tiles across all the targets in our pipeline

TargetScan, ReceptorScan, EpitopeScan, T-Fish, & SafetyScan used to generate ImmunoBank of de-risked antigens/TCRs

Suite of TScan Discovery Technologies

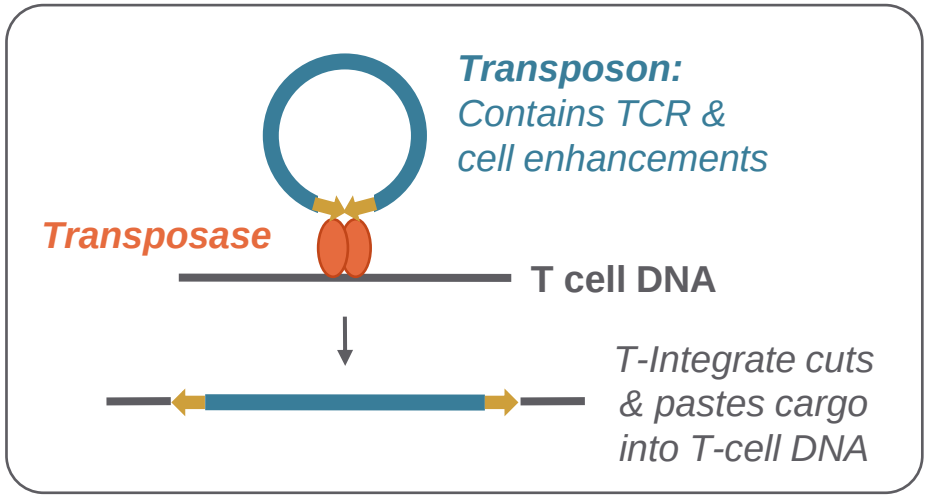
- TargetScan
- ReceptorScan
- T-Fish
- EpitopeScan
- SafetyScan

ImmunoBank of Therapeutic Antigens/TCRs



T-Integrate technology overcomes lentiviral constraints - enables TCR-T multiplexing and T cell enhancements

T-Integrate:
Genetic Cargo Delivery System



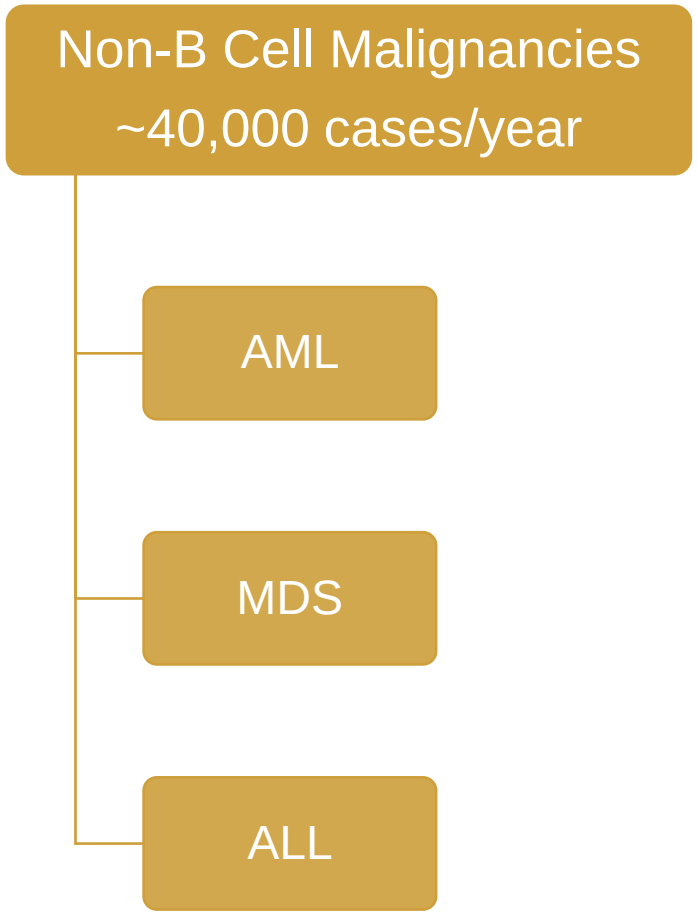
*Transposon/transposase technology enables delivery of the **TCR** as well as many **cell enhancements** (e.g., CD8α/β, TGFβR2dn, purification tags)*

Advantages of T-Integrate non-viral delivery over lentivirus:

- Greater cargo size enables delivery of T cell functional enhancements
- Rapid process development
- Cost-effective manufacturing

Clinical Programs:
Liquid Tumor Program

TCR-T uniquely addresses myeloid leukemias

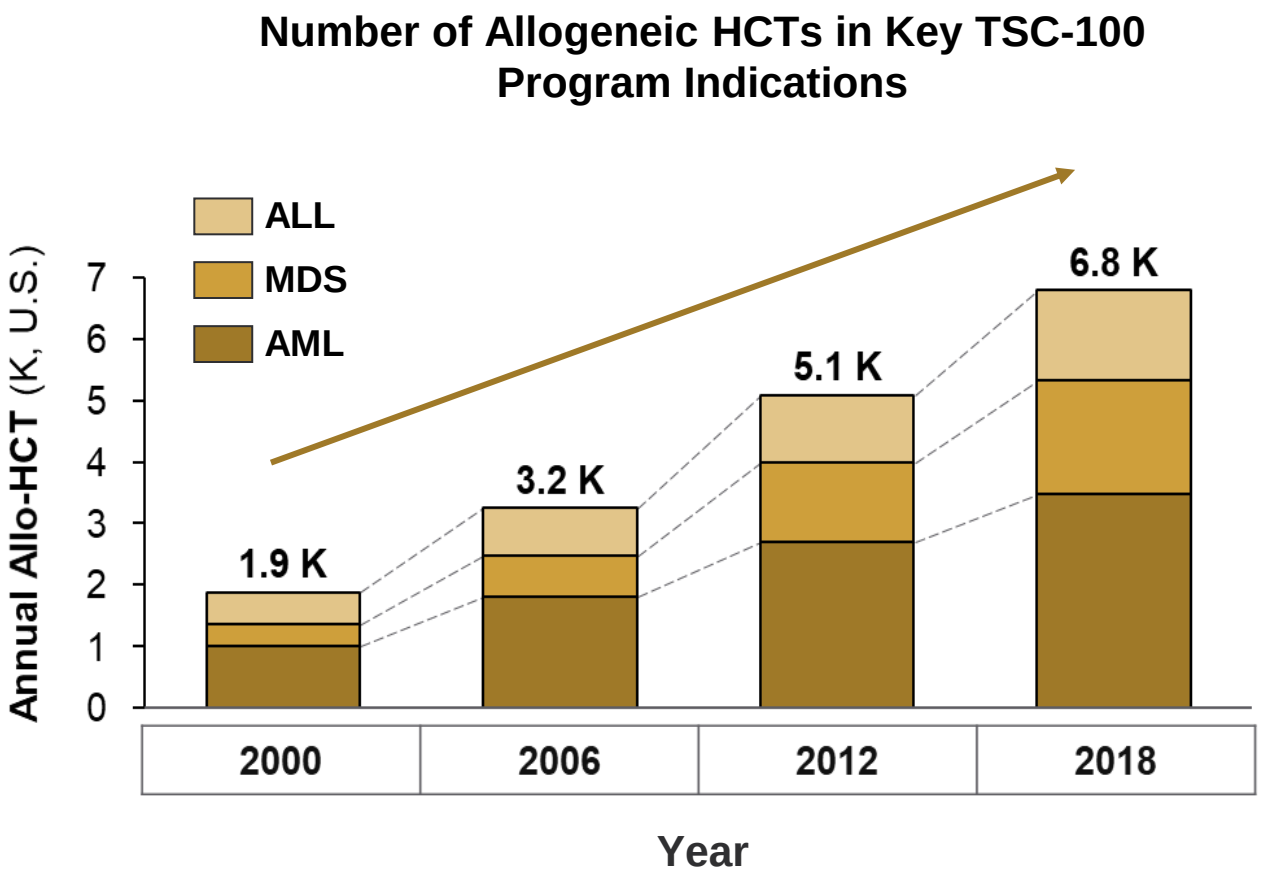


- Not addressable by CAR-T therapy
- Transplant is considered curative for many and is expected to remain standard of care
- ~40% of patients relapse post-transplant with few treatment options (~90% mortality within 1 year of relapse)

TScan program is designed to prevent relapse in patients undergoing HCT

Source: Independent KOL market research conducted June 2020.

Growing unmet transplant need in myeloid leukemias



Currently ~7,000 patients annually in the U.S. undergo allogeneic transplant

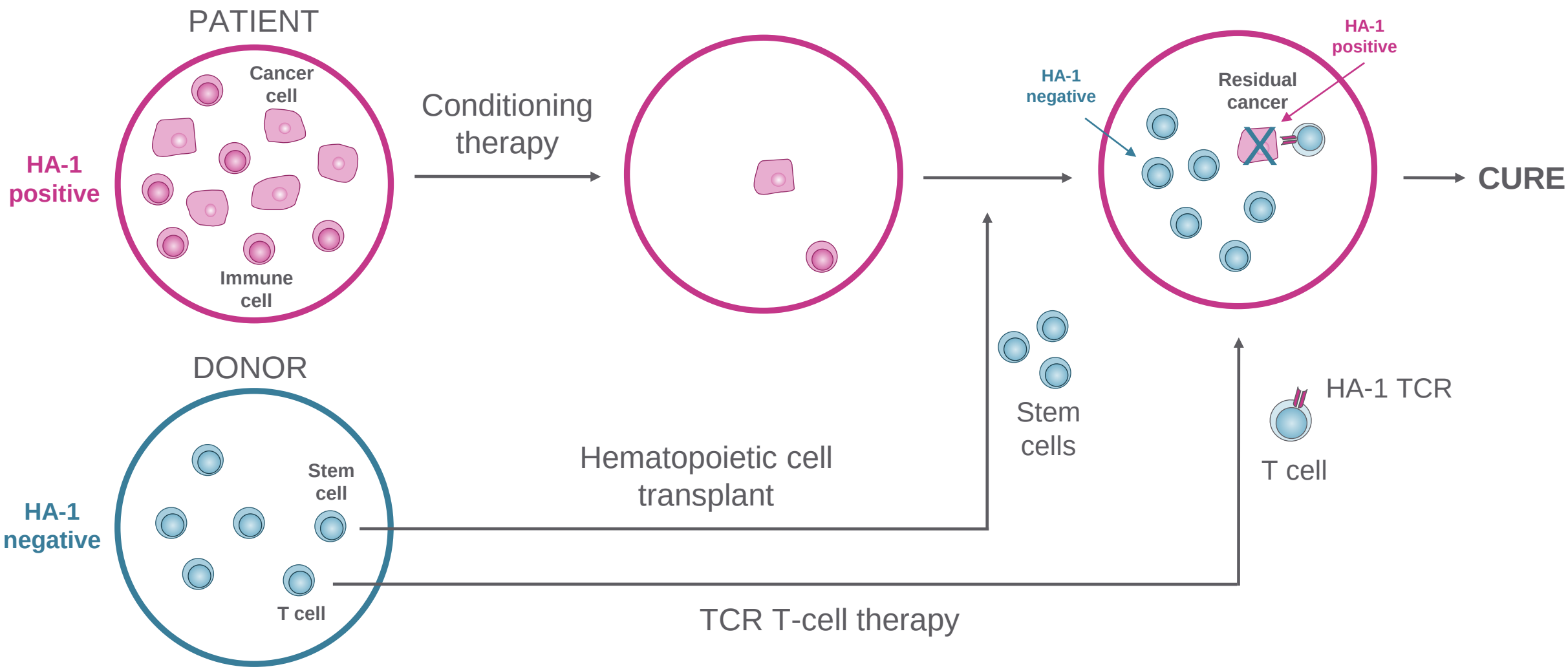
Transplant use has been increasing ~7% per year for the past 20 years

Market anticipated to grow as novel agents bring more patients to remission, qualifying them for HCT

If successful, physicians may transplant patients that aren't in complete remission, further expanding the market

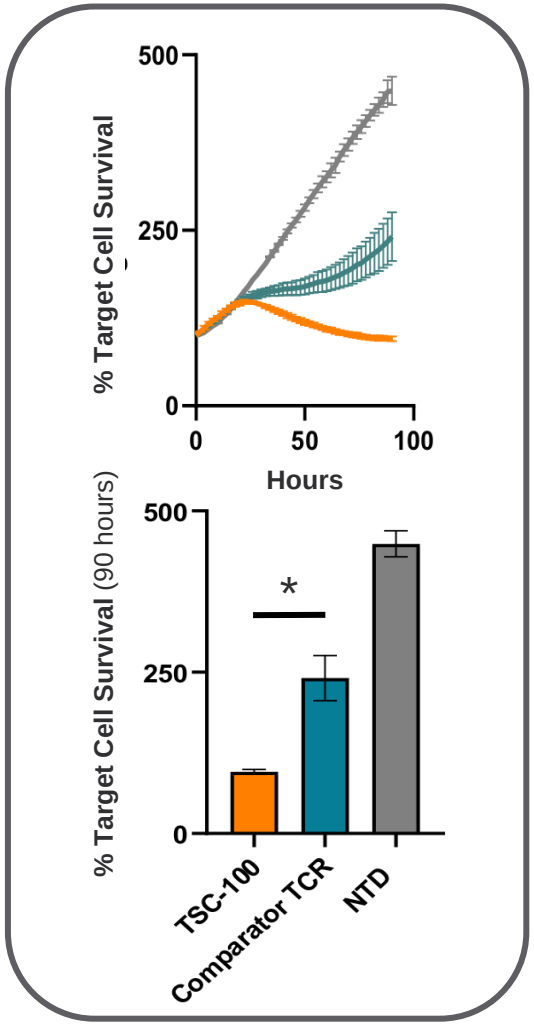
Source: Independent KOL market research conducted June 2020.

Eliminate residual cancer by targeting blood-specific antigens

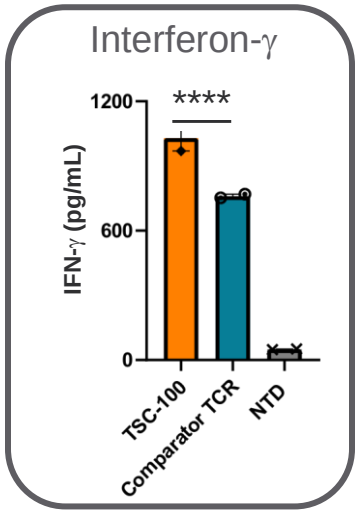


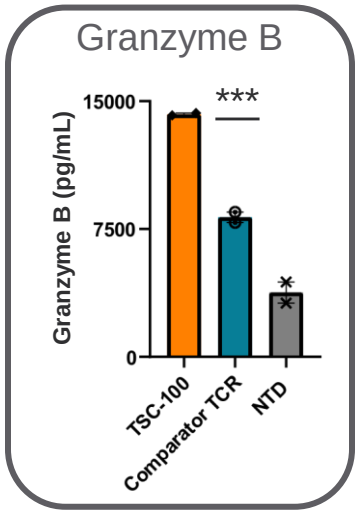
TSC-100 has superior activity relative to comparator HA-1 TCR

Cytotoxicity

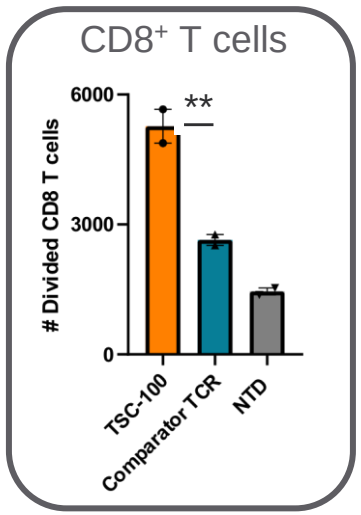


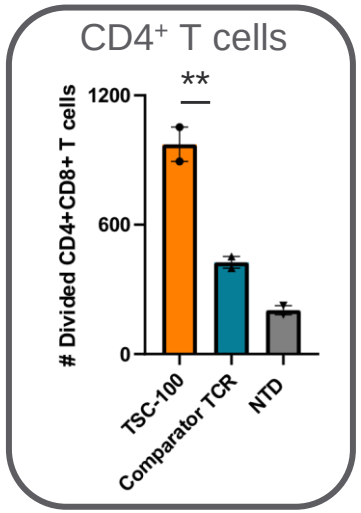
Cytokine Production



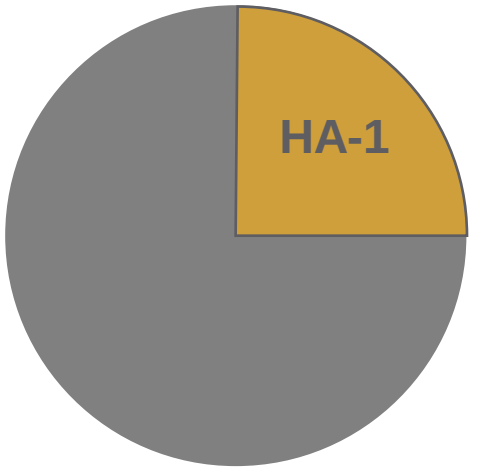


T Cell Proliferation



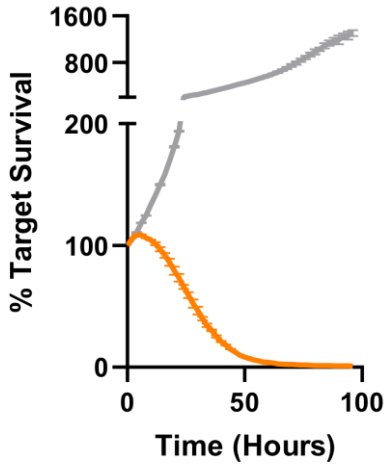


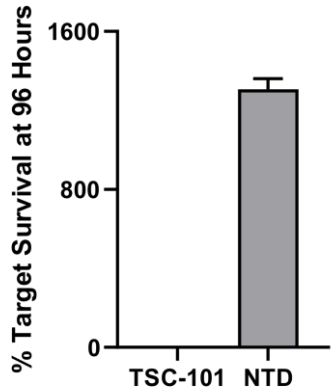
HA-1-positive
25% of allo-HCT



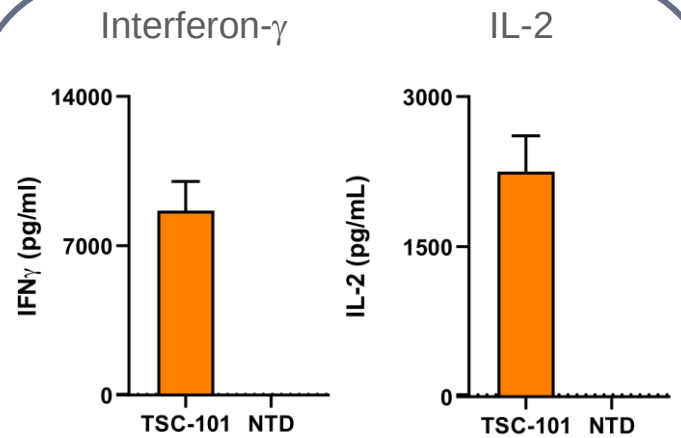
TSC-101 is highly active and comparable to TSC-100

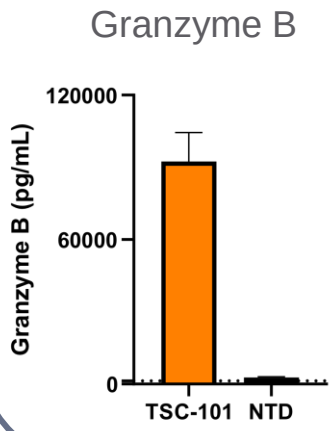
Cytotoxicity

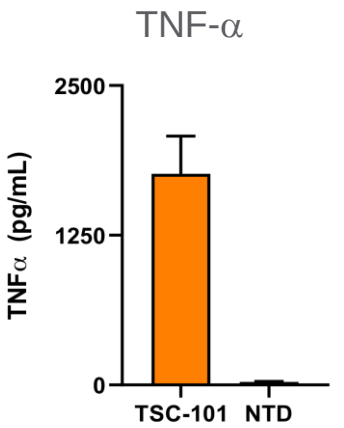




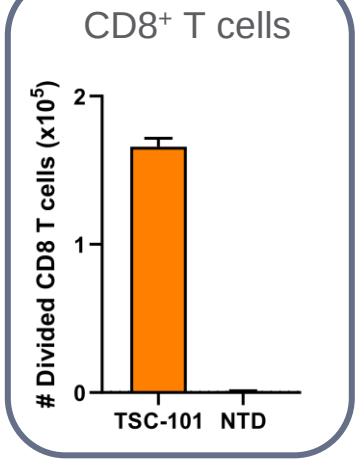
Cytokine Production

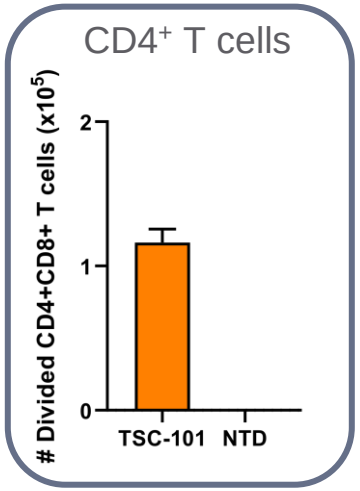




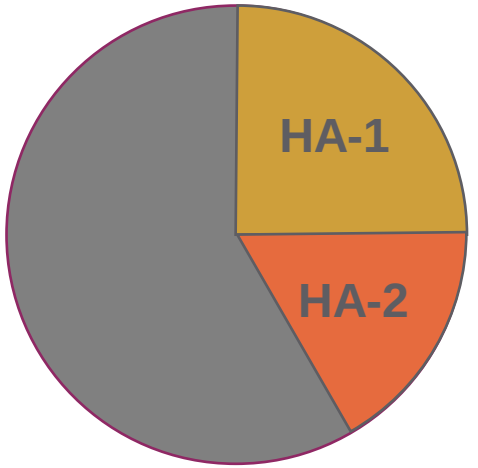


T cell Proliferation





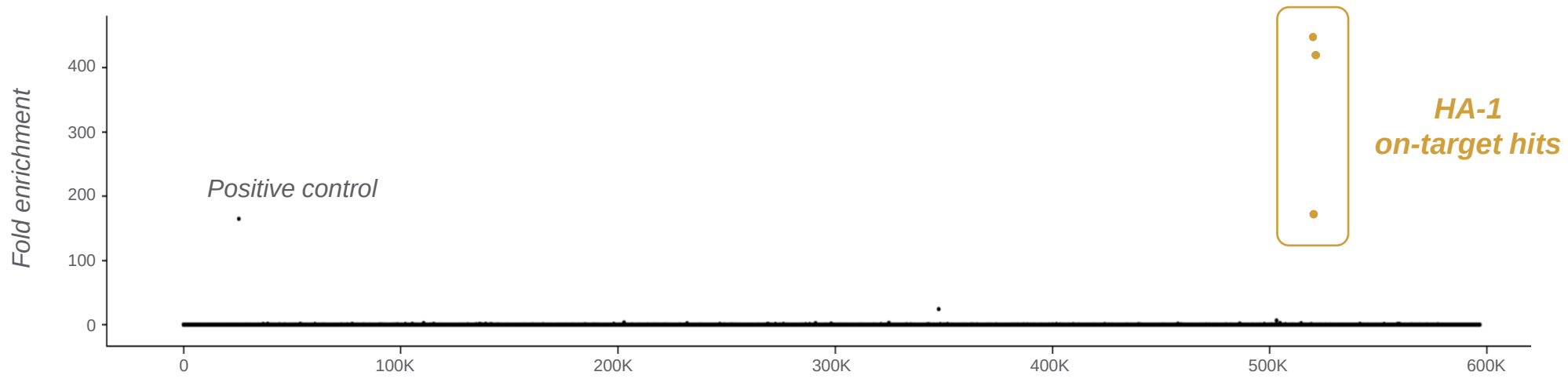
HA-1- or HA-2-positive
40% of allo-HCT



TSCAN THERAPEUTICS

TSC-100 SafetyScan screen shows no material off-targets

Off-target SafetyScan Data



- SafetyScan revealed **no significant off-targets** for the TSC-100 TCR
- TSC-100 demonstrated no cross-reactivity or alloreactivity

Liquid tumor program on track for multi-arm Phase 1 trial

Treatment arms

RIC Haploidentical donor transplant + TSC TCR-T

Patient A*02:01 positive
(~42% US pop)

Patient HA-1 positive
(~60%)

Donor
A*02:01 positive, HA-1 negative
or A*02:01 negative

TSC-100
Monotherapy

Patient HA-1 negative,
HA-2 positive
(~40%)

Donor
A*02:01 negative

TSC-101
Monotherapy

Control arm

RIC Haploidentical donor transplant alone

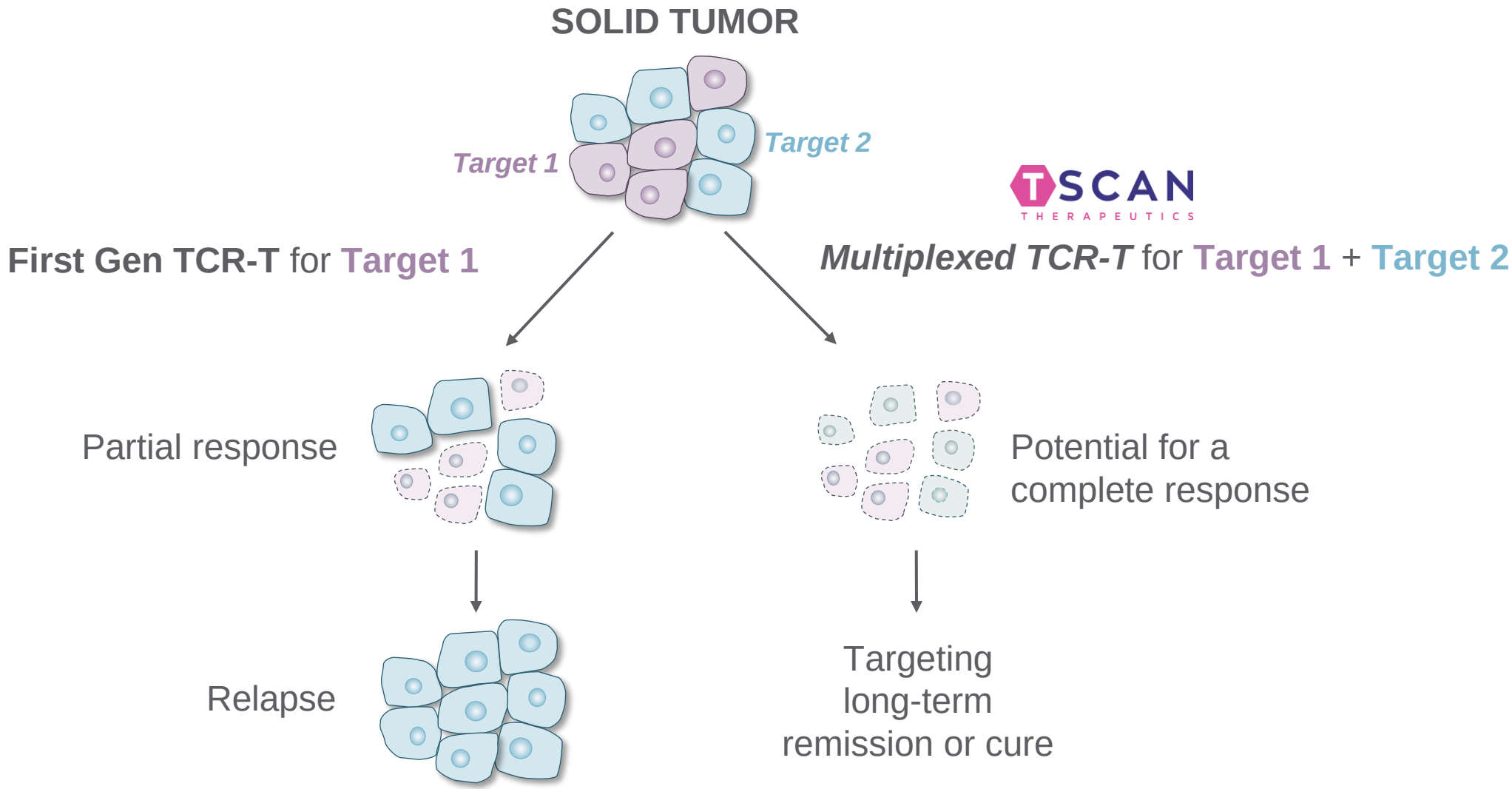
Patient A*02:01 negative
(~58% US pop)

Standard-of-care

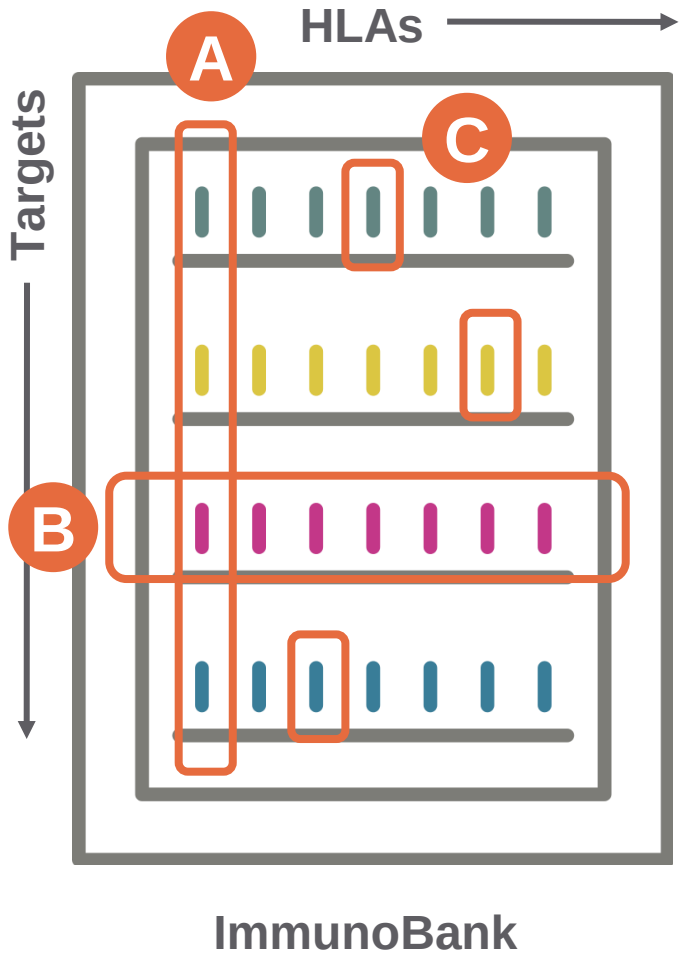
Surrogate markers include donor chimerism and minimal residual disease

Clinical Programs:
Solid Tumor Program

Multiplexing overcomes the problem of tumor heterogeneity



Multiplexing addresses resistance and expands market

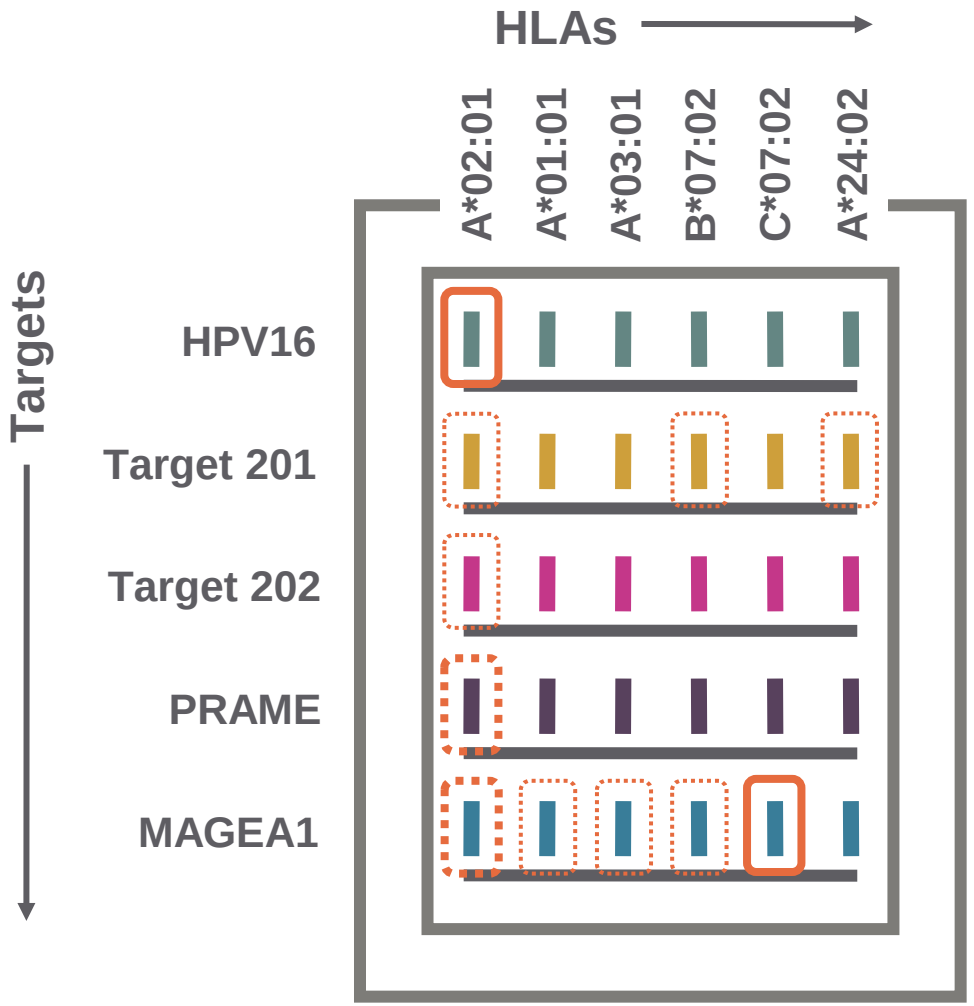


A Multiplexing across targets addresses the problem of tumor heterogeneity

B Multiplexing across HLAs prevents resistance due to HLA loss / mutation

C Multiplexing across both is the ultimate solution, but requires a well-populated ImmunoBank

We are building our pipeline to enable multiplexed therapy in solid tumors



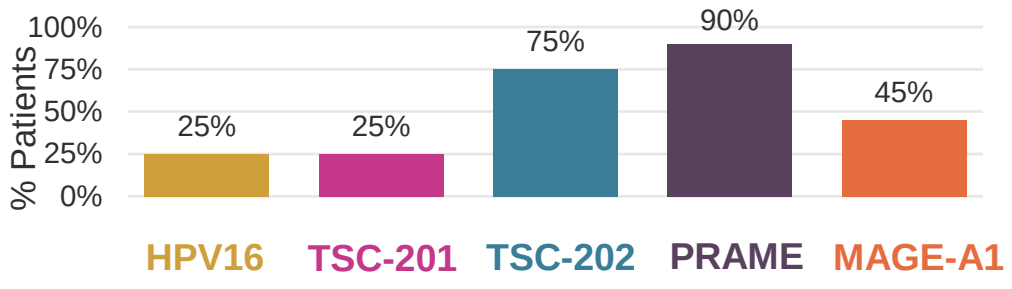
Frequency of HLA positivity in the U.S.

HLA Allele	Population percentage
HLA-A*01:01	23%
HLA-A*02:01	**42%**
HLA-A*03:01	21%
HLA-A*11:01	12%
HLA-A*24:02	16%
HLA-B*07:02	20%
HLA-C*04:01	25%
HLA-C*07:01	27%
HLA-C*07:02	**25%**

Programs address major unmet needs in ‘hot’ solid tumors

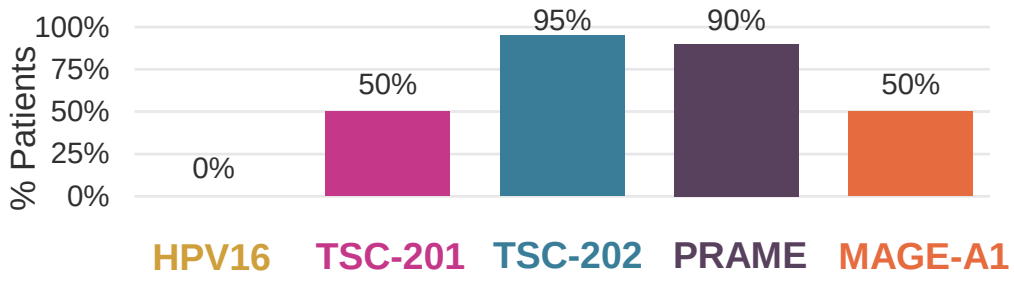
Head & Neck

66 K Incident Patients in U.S.



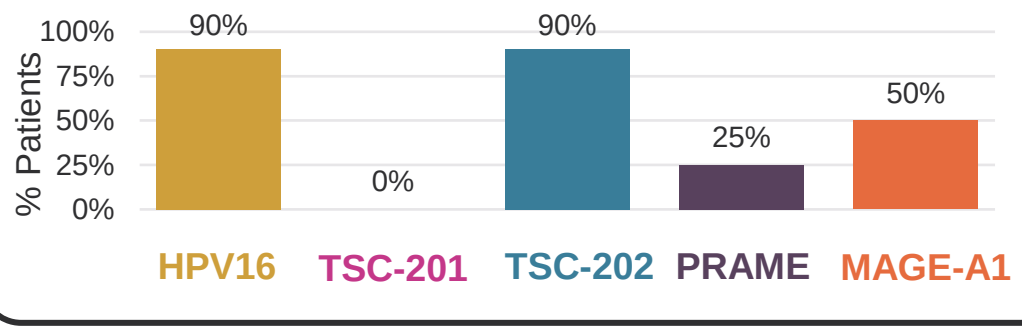
Melanoma

100 K Incident Patients in U.S.



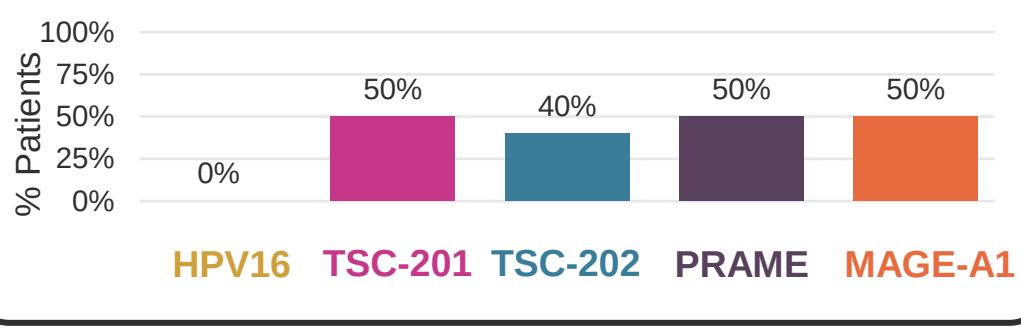
Cervical (Uterine cervix)

15 K Incident Patients in U.S.



NSCLC

230 K Incident Patients in U.S.

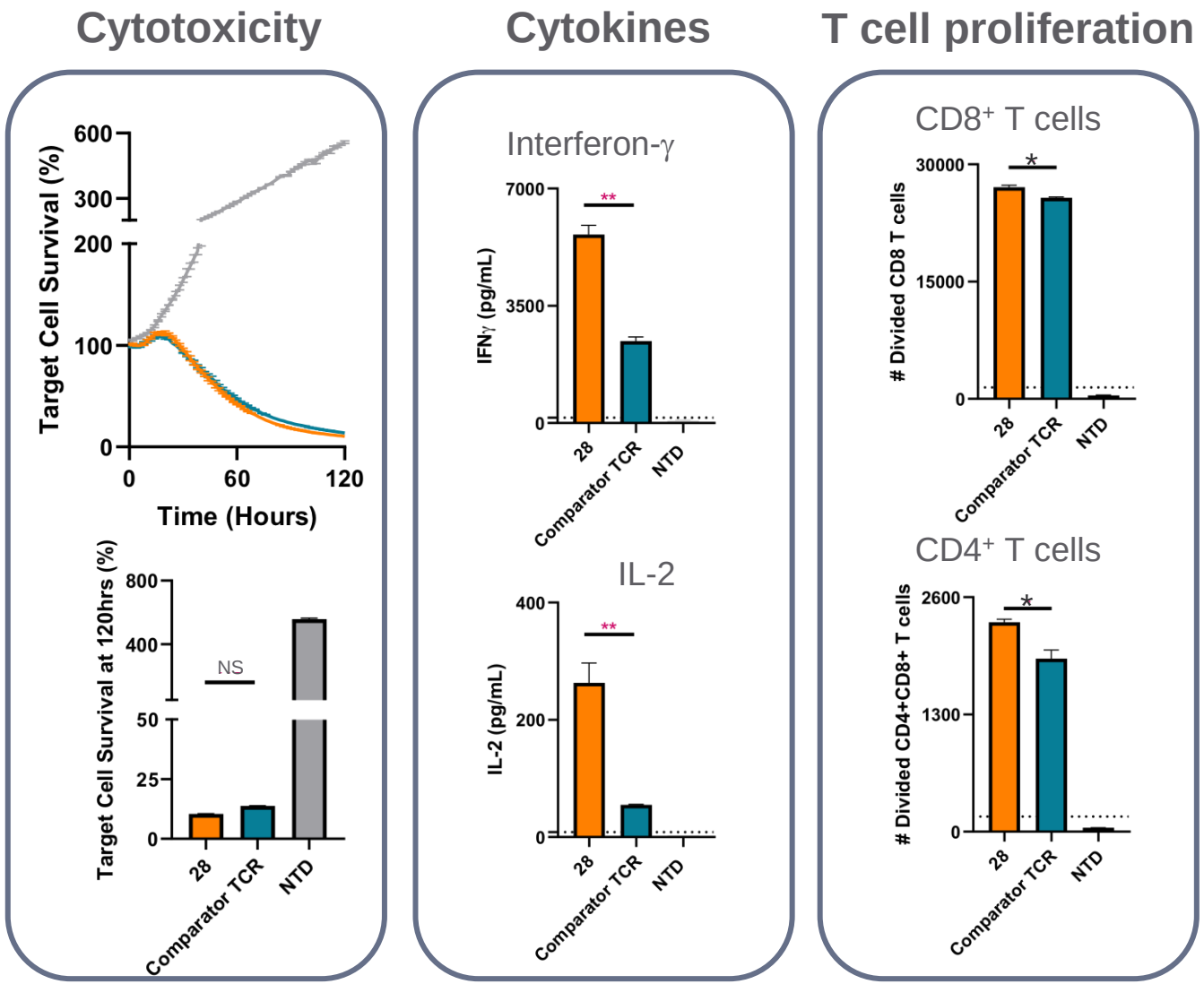


*Denotes broad lung cancer expression.
Source: American Cancer Society

HPV TCR shows superior activity vs. comparator TCR

TSC-200

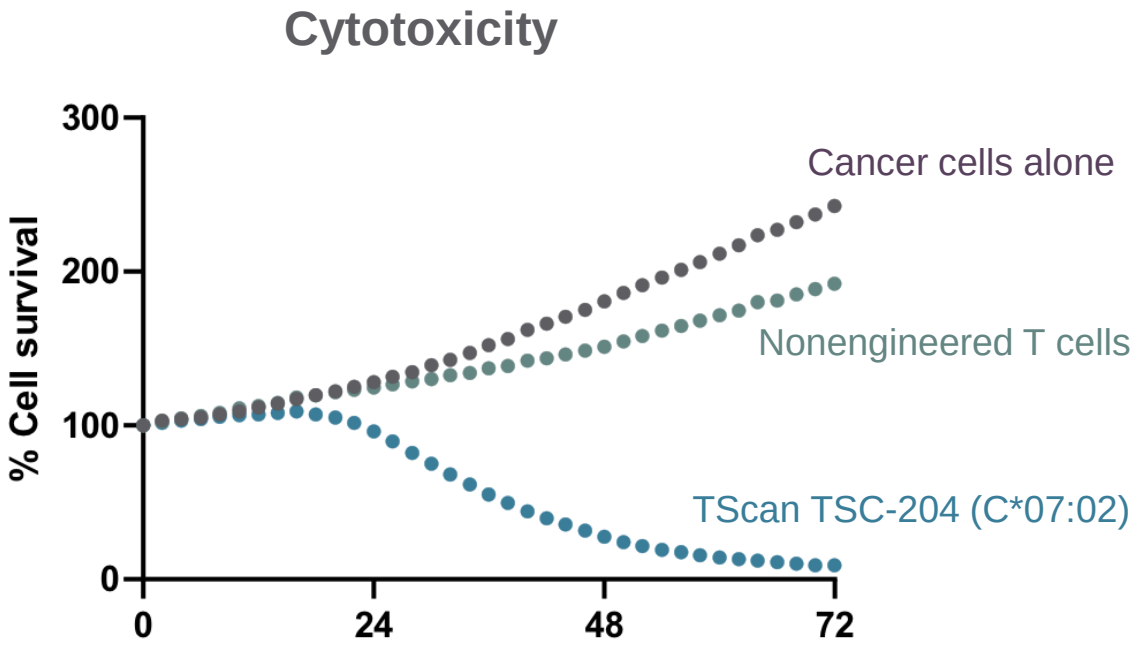
- HPV is an oncogenic virus found in many solid tumors
- A Phase I trial at the NCI showed an ORR of 50% with a single HPV TCR
- TScan will develop TSC-200 as an *enhanced* TCR-T cell product



MAGE-A1 TCR discovered from patient responding to ICI Rx

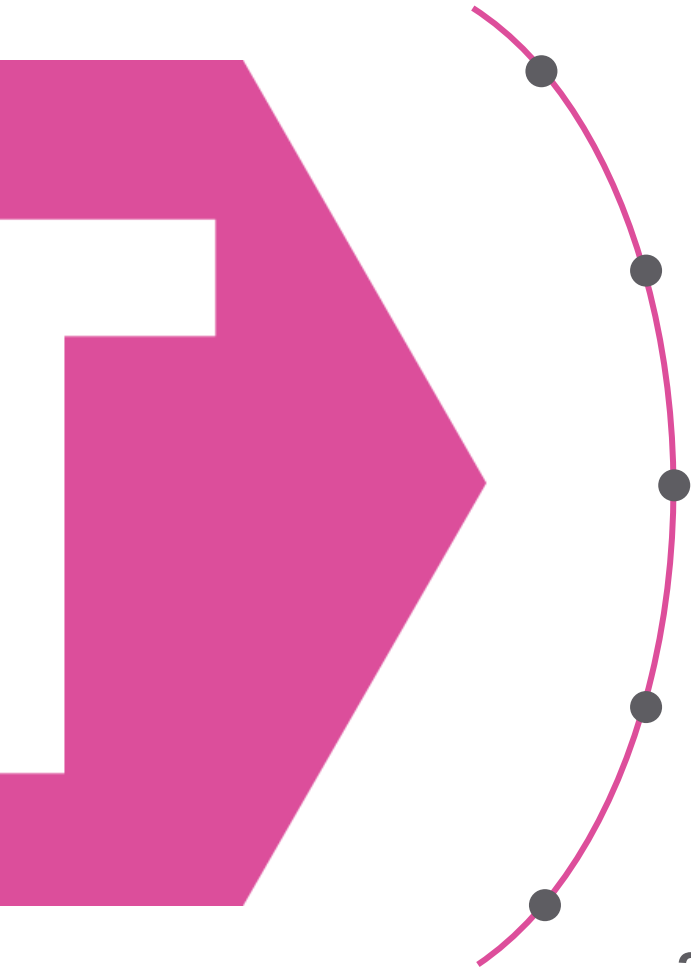
TSC-204

- Discovered from a patient with Head & Neck cancer who responded to immunotherapy
- MAGE-A1 is a cancer testis antigen expressed in many solid tumors
- TSC-204 recognizes a *novel antigen* for a common HLA type (C*07:02)
- Phase I trials of MAGE-A1 TCRs show promising response rates



TScan is expanding MAGE-A1 program to include *additional HLA types*

TScan highlights



- Transformative Platform to Discover the Natural Targets of T cells
- Platform Enables Enhanced Multiplexed TCR-T cell Therapy
- Two INDs Filed in 2021; Additional INDs Planned for 2022
- Strategic Target Discovery Partnership with Novartis
- Cash Position of $140.8 MM as of 3/31/2022 Funds Company into 2024