Unleash Immunity

TScan ASH 2021 Highlights
December 15, 2021

Disclaimers and Forward-Looking Statements

This presentation and the accompanying oral presentation contain forward-looking statements. All statements other than statements of historical fact contained in this presentation, including statements regarding possible or assumed future results of operations of TScan Therapeutics, Inc. (the "Company", “we”, “our” and “us”), expenses and financing needs, business strategies and plans, research and development plans or expectations, the structure, timing and success of the Company’s planned preclinical development and clinical trials, expected milestones, market sizing, competitive position, regulatory matters, industry environment and potential growth opportunities, among other things. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “anticipate,” “project,” “target,” “design,” “estimate,” “predict,” “potential,” “plan” or similar expressions or the negative of those terms. The Company has based these forward-looking statements largely on its current expectations and assumptions and on information available as of the date of this presentation. The information in this presentation is provided only as of November 9, 2021, and the Company assumes no obligation to update any forward-looking statements after the date of this presentation, except as required by law.

The forward-looking statements contained in this presentation and the accompanying oral presentation are subject to known and unknown risks, uncertainties, assumptions and other factors that may cause actual results or outcomes to be materially different from any future results or outcomes expressed or implied by the forward-looking statements. These risks, uncertainties, assumptions and other factors include, but are not limited to, including the development, clinical and regulatory plans or expectations for the Company’s TCR-T therapy candidates, assumptions and uncertainties regarding the impact of the continuing COVID-19 pandemic on the Company’s business, operations, strategy, goals and anticipated timelines, as well as the risks described in the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of the Company's Final Prospectus for its initial public offering, which is on file with the Securities and Exchange Commission (SEC) and available on the SEC's website at www.sec.gov. Additional factors may be described in those sections of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, filed with the SEC in the fourth quarter of 2021. You should not put undue reliance on any forward-looking statements. Forward-looking statements should not be read as a guarantee of future performance or results and will not necessarily be accurate indications of the times at, or by, which such performance or results will be achieved, if at all. It is not possible for the Company to predict all risks, nor can the Company assess the impact of all factors on its business or the markets in which it operates or the extent to which any factor, or combination of factors, may cause actual results or outcomes to differ materially from those contained in any forward-looking statements the Company may make.

Agenda

Welcome and Introduction

- David Southwell, CEO

Preclinical Data for TSC-100 & TSC-101

- Gavin MacBeath, Ph.D., CSO

Clinical Study Design

- Shrikanta Chattopadhyay, M.D., VP Medical

The Unmet Need and Standard of Care

- Yi-Bin Chen, M.D., M.S., Director, Hematopoietic Cell Transplant & Cell Therapy Program, Rogers Endowed Chair, MGH, Associate Professor of Medicine, Harvard Medical School

Questions & Answers

Presenters

Yi-Bin Chen, M.D., M.S.

- Director, Hematopoietic Cell Transplant and Cell Therapy Program
- Allan B. Rogers, Jr. and Cara J. Rogers Endowed Chair, Massachusetts General Hospital
- Associate Professor of Medicine, Harvard Medical School

David Southwell
CEO

Gavin MacBeath, Ph.D.
CSO

Shri Chattopadhyay
MD; VP, Medical

TScan Technology

Gavin MacBeath, Ph.D.

TCR therapy eliminates residual cancer by targeting patient-specific peptide sequences expressed on leukemia cells

HA-1^{+} & HLA-A*02:01^{+}

*HA-1^{+} target peptide is presented by HLA-A*02:01*

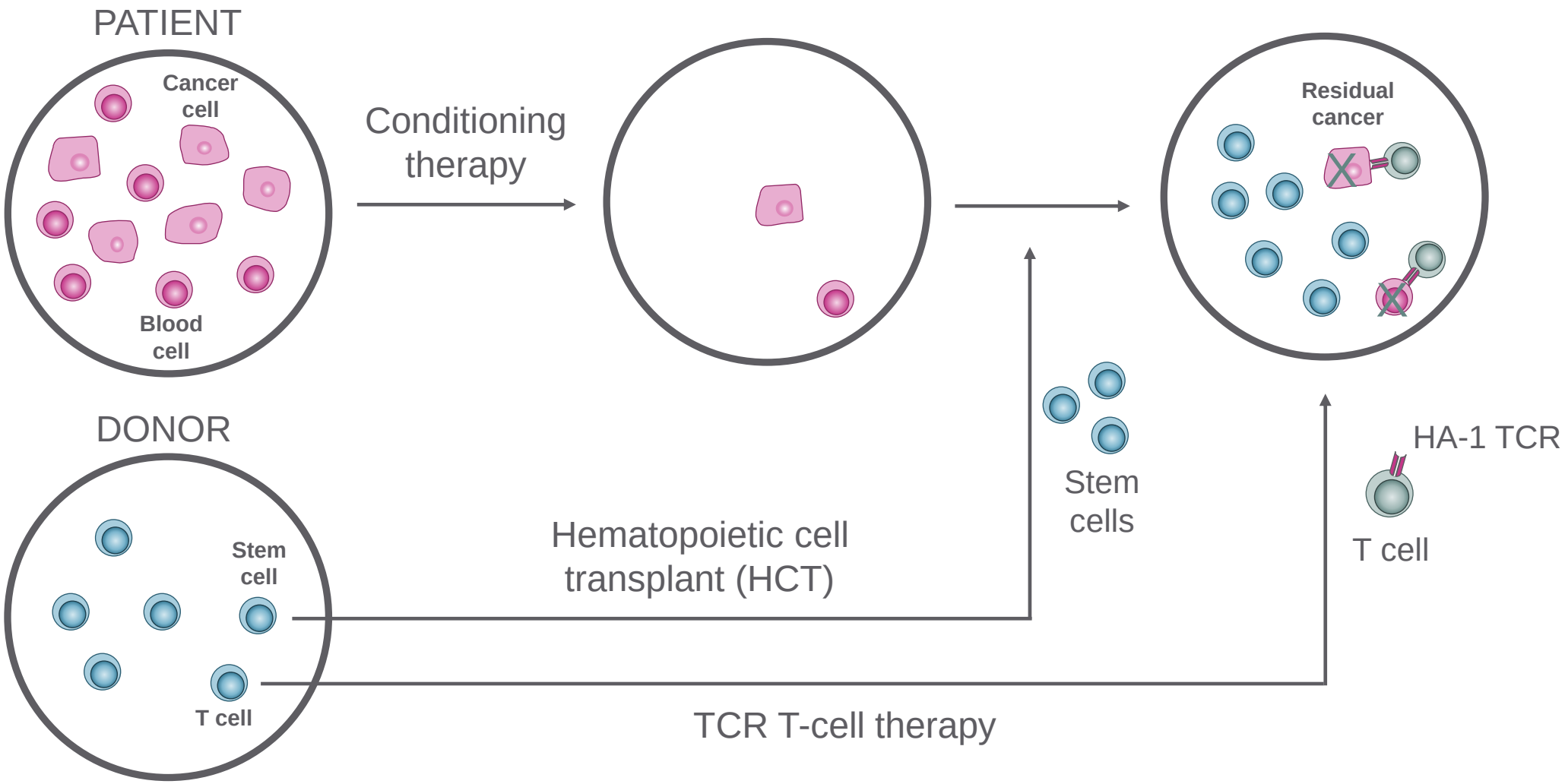
VL**H**DDLLEA

(derived from ARHGAP45)

HA-1^{-} and/or HLA-A*02^{-} donor

*HA-1^{-} target peptide is not presented by HLA-A*02:01*

VL**R**DDLLEA



HA-1 and HA-2 were discovered in patients with graft-versus-leukemia effect from donor T cells

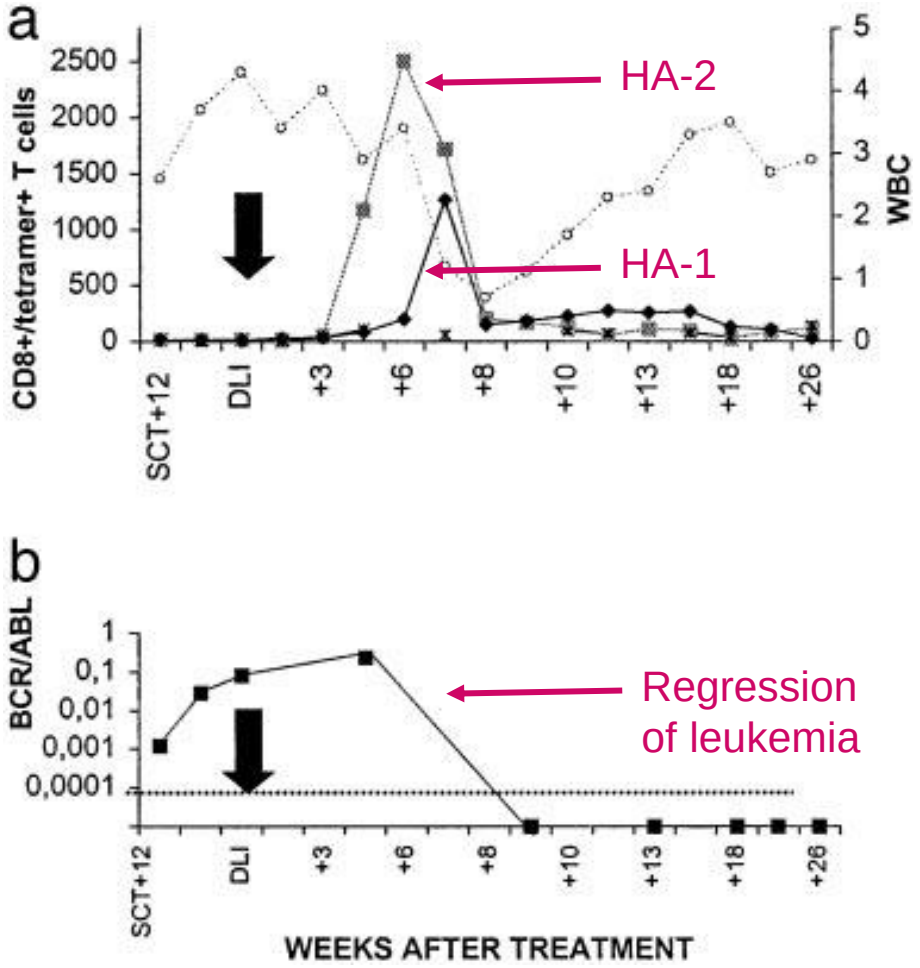
Hematopoiesis-restricted minor histocompatibility antigens HA-1- or HA-2-specific T cells can induce complete remissions of relapsed leukemia

W. A. Erik Marijt*†, Mirjam H. M. Heemskerk*, Freke M. Kloosterboer*, Els Goulmy‡, Michel G. D. Kester*, Menno A. W. G. van der Hoorn*, Simone A. P. van Luxemburg-Heys*, Manja Hoogeboom*, Tuna Mutis‡, Jan Wouter Drijfhout‡, Jon J. van Rood§, Roel Willemze*, and J. H. Frederik Falkenburg*

Departments of *Hematology and ‡Immunohematology and Blood Transfusion, Leiden University Medical Center, PO Box 9600, 2300 RC, Leiden, The Netherlands; and §Europdonor Foundation, 2333 BZ, Leiden, The Netherlands

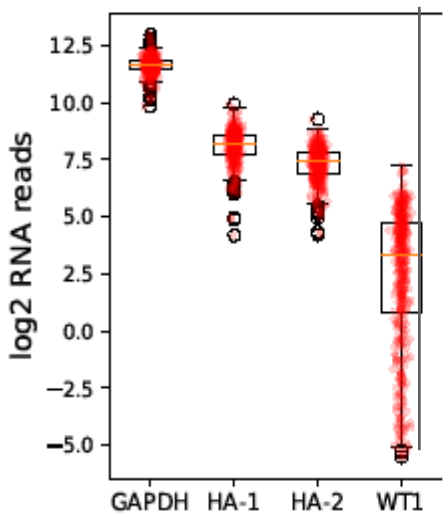
Proc Natl Acad Sci USA (2003) **100**, 2743.

- HA-1 and HA-2-specific T cells expand in a patient that had relapsed following HSC transplant and received a donor lymphocyte infusion (DLI)
- Expansion of HA-1 and HA-2-specific T cells is immediately followed by complete regression and conversion to 100% donor chimerism

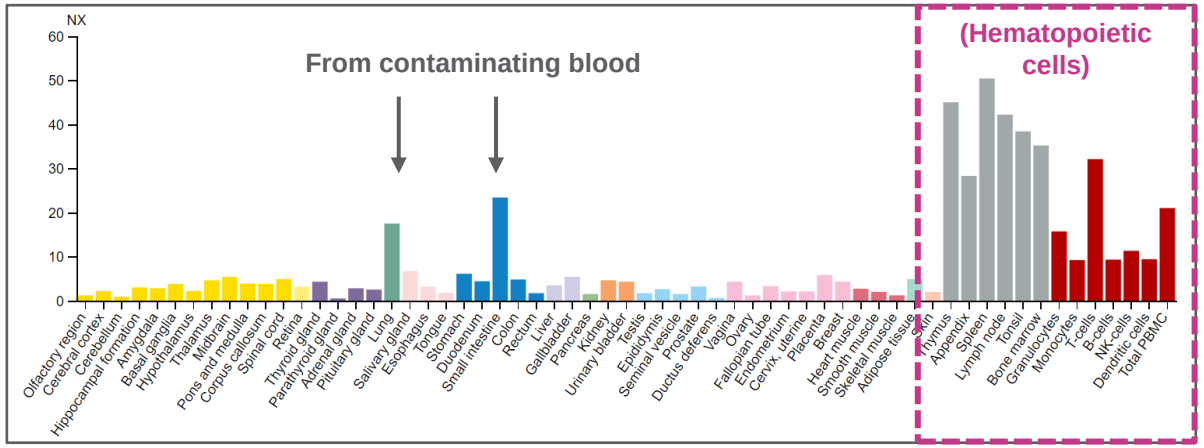


HA-1 and HA-2 are highly expressed in normal and malignant blood cells but not normal tissues

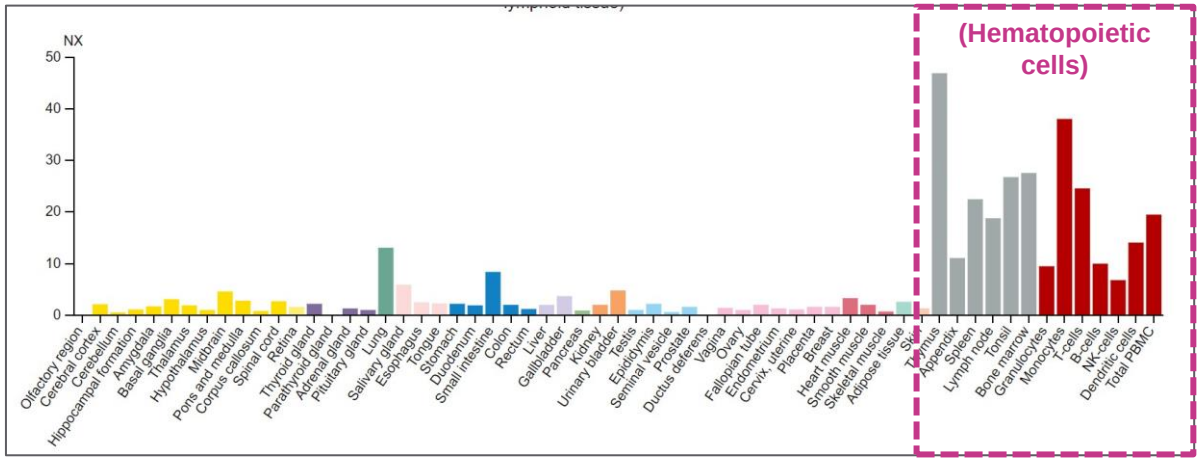
Target Expression in AML



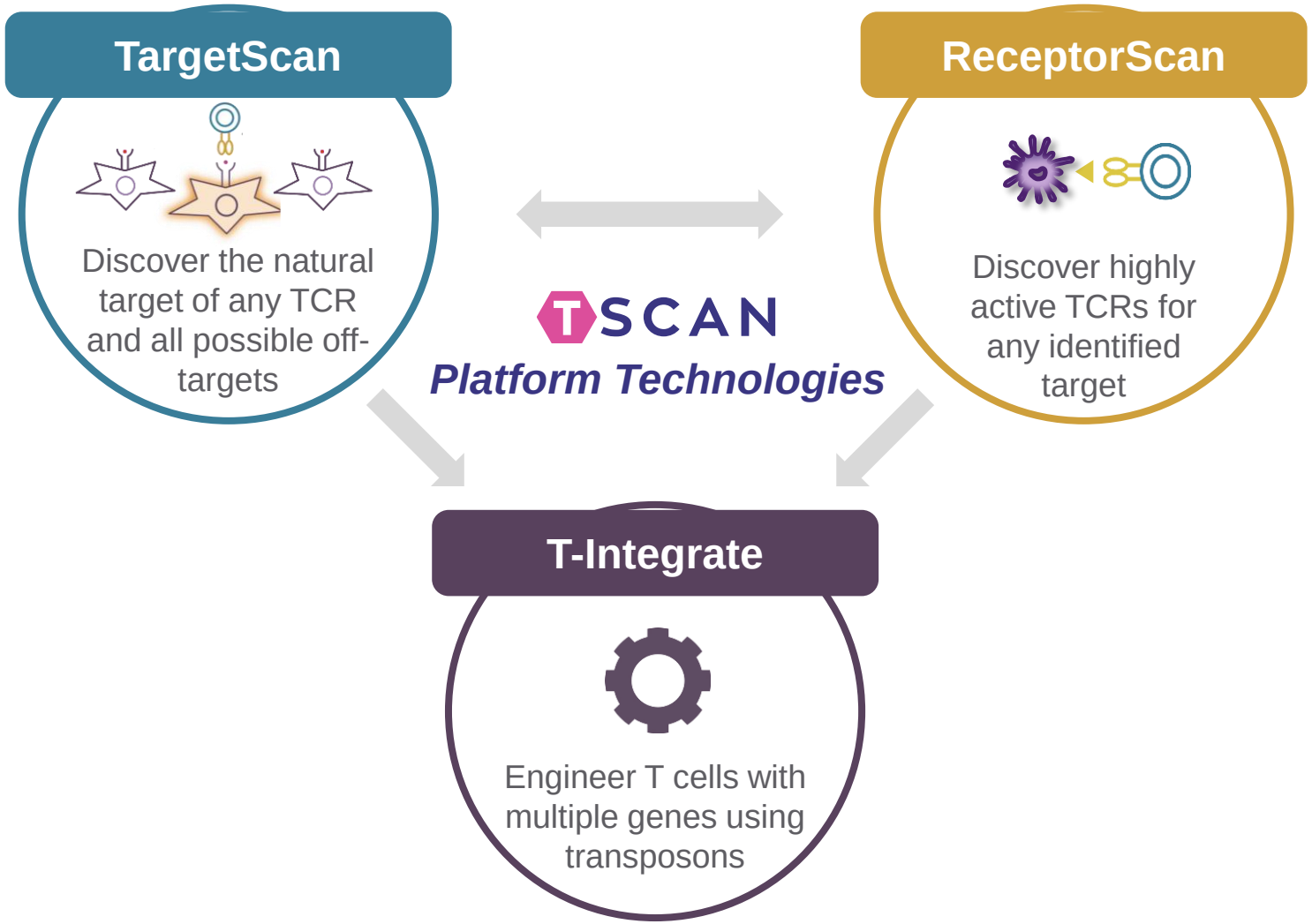
HA-1 Expression in Normal Tissue



HA-2 Expression in Normal Tissue

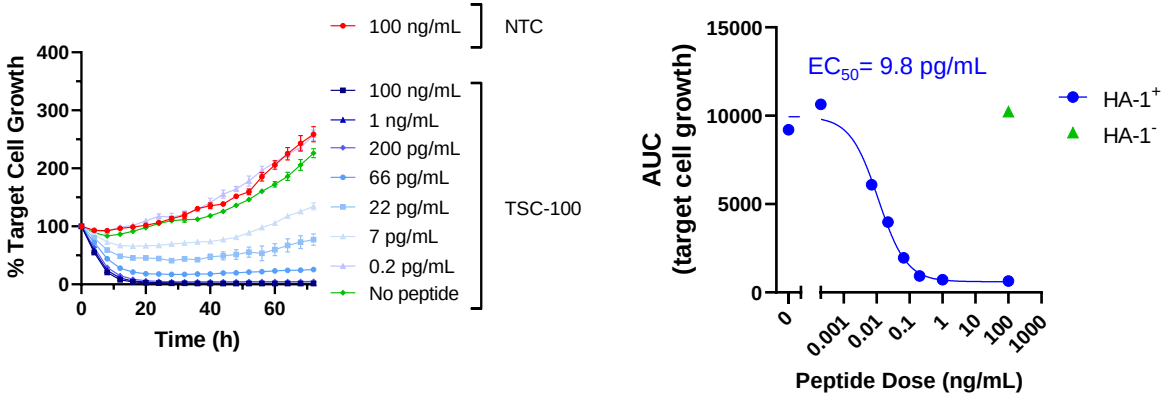


TSC-100 and TSC-101 were discovered using TScan's platform technology



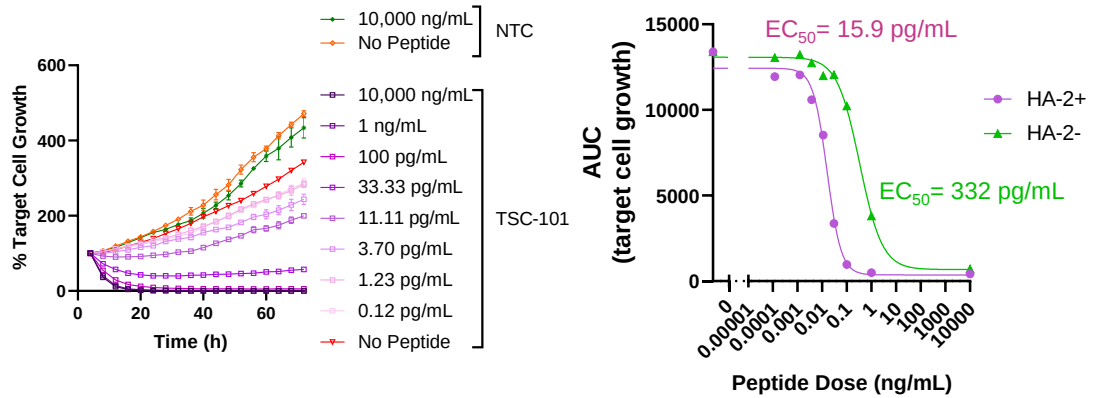
TSC-100 and TSC-101 recognize their targets (HA-1 and HA-2) with very high avidity

TSC-100



EC_{50}= 9.8 pg/mL

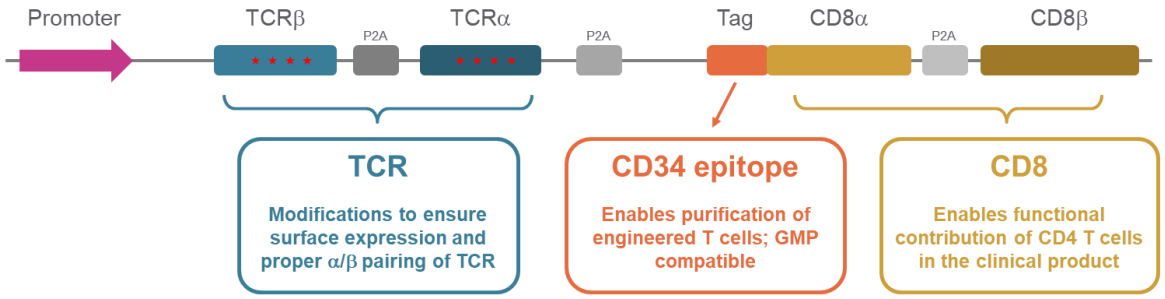
TSC-101



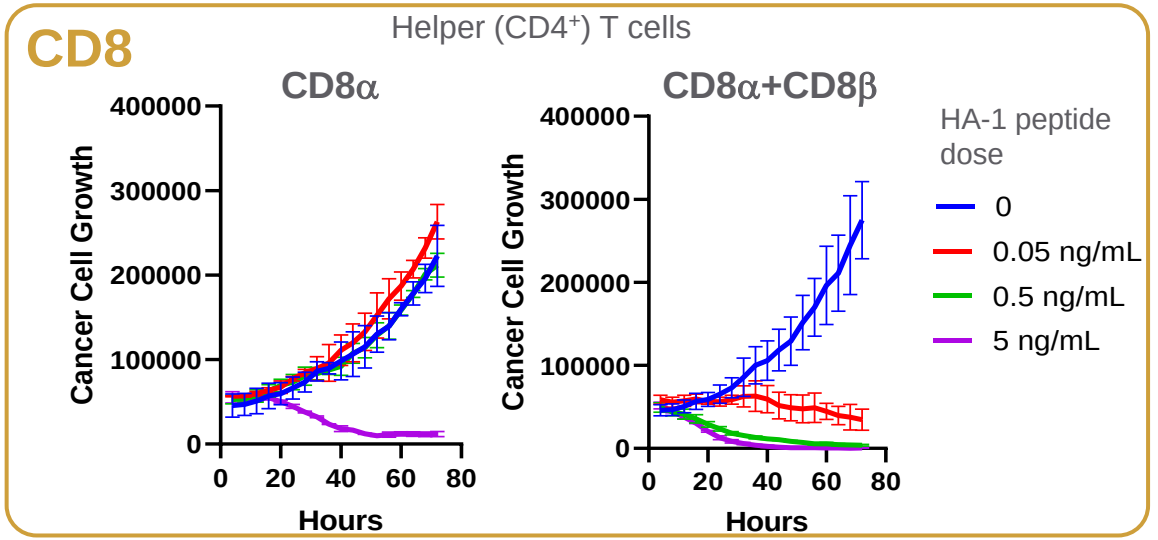
EC_{50}= 15.9 pg/mL

Delivery vector generates enhanced T cell product that includes both helper T cells and cytotoxic T cells

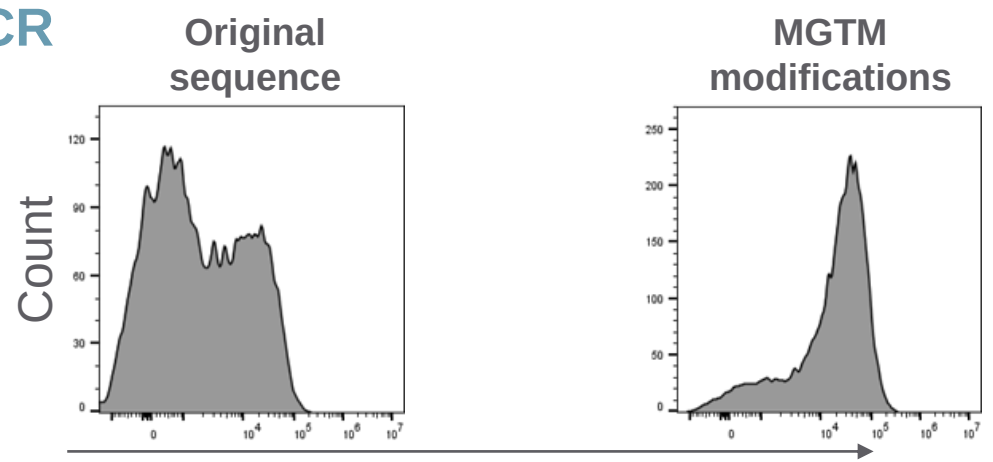
TScan delivery vector



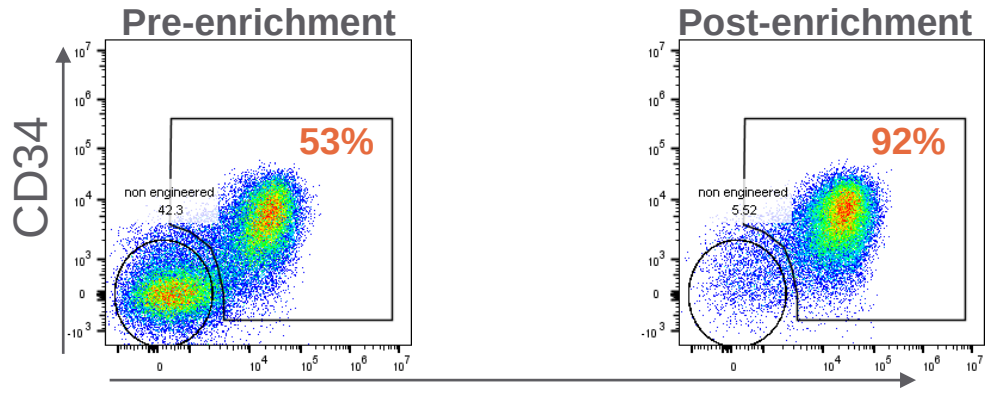
CD8



TCR

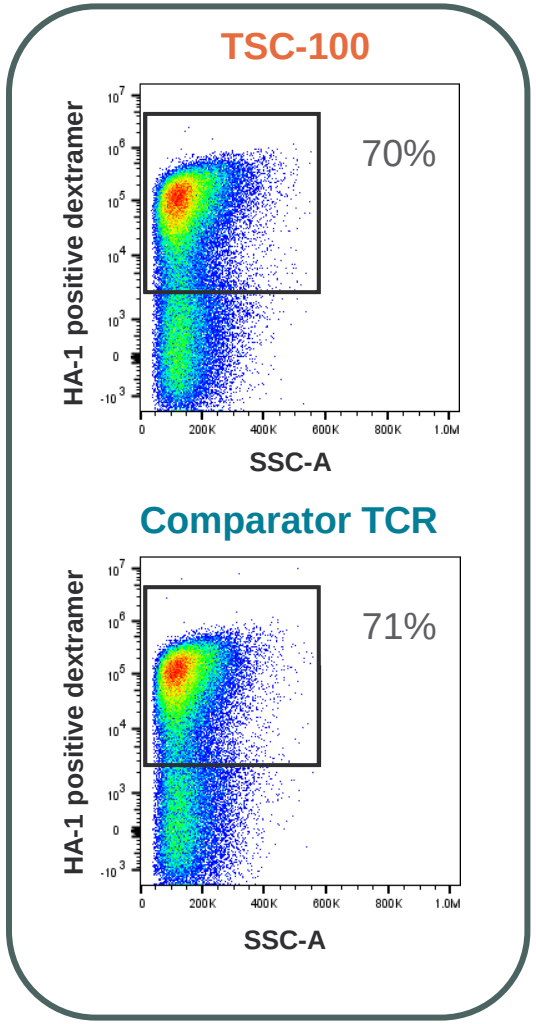


CD34 tag

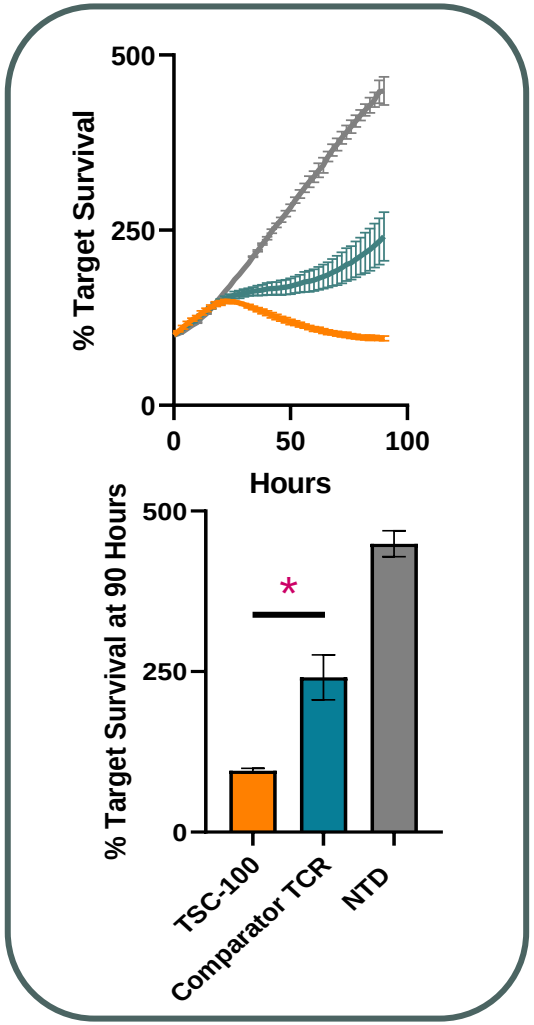


TSC-100 has superior pre-clinical activity relative to comparator HA-1 TCR

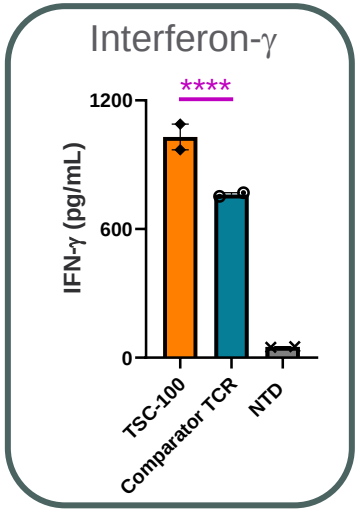
Expression

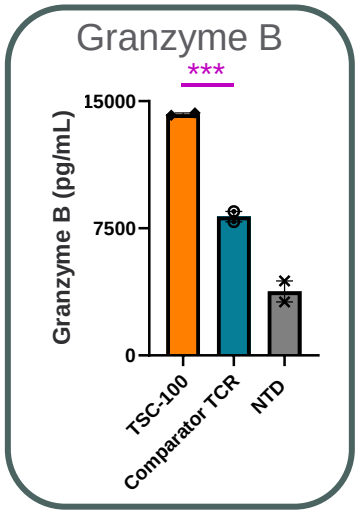


Cytotoxicity

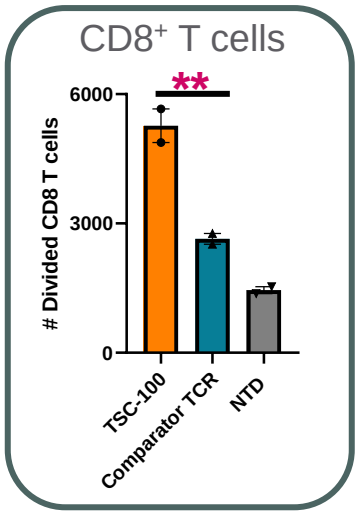


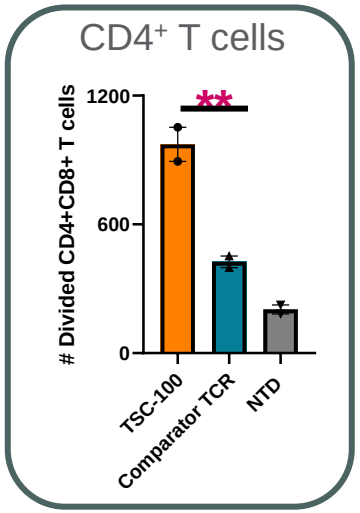
Cytokine production





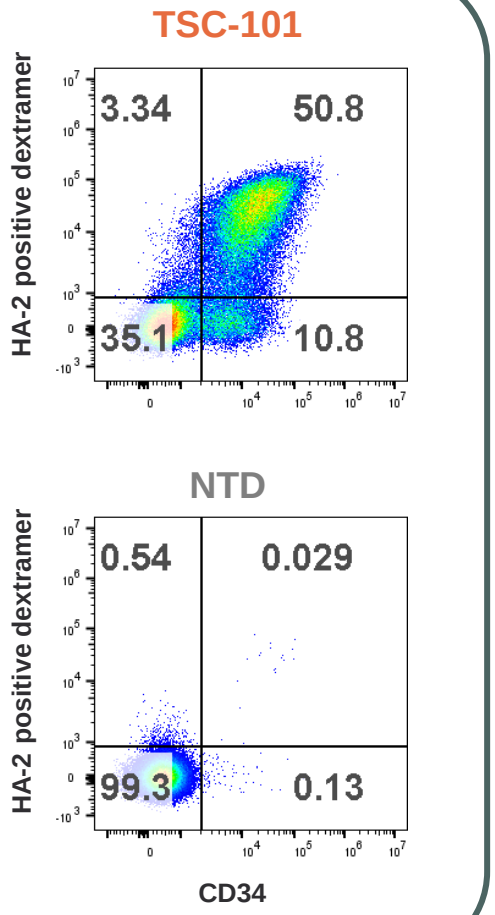
T cell proliferation



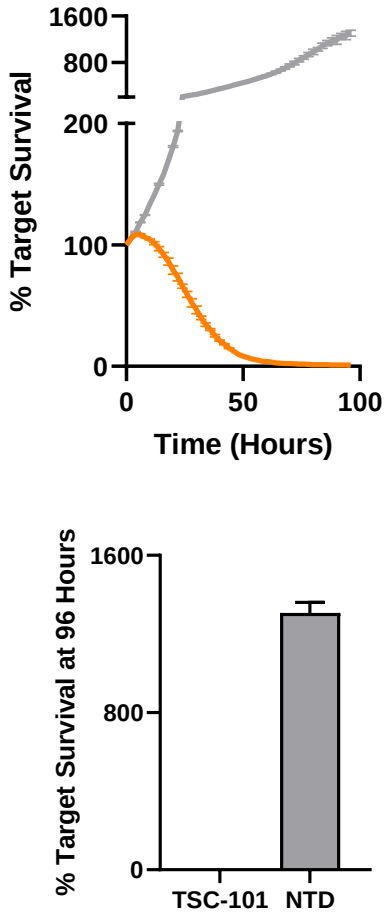


TSC-101 has high activity similar to TSC-100

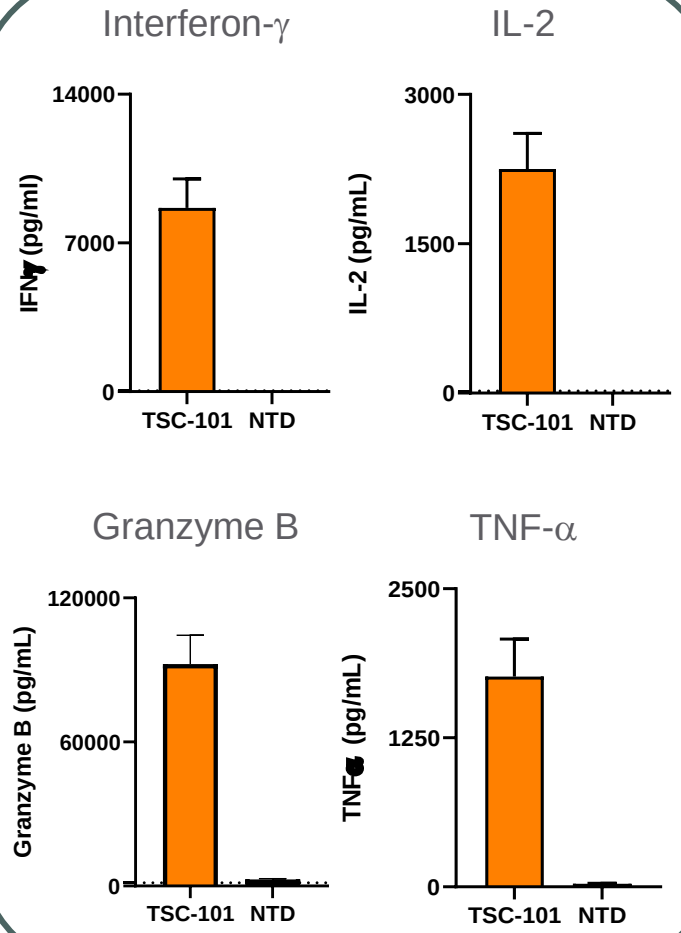
Expression



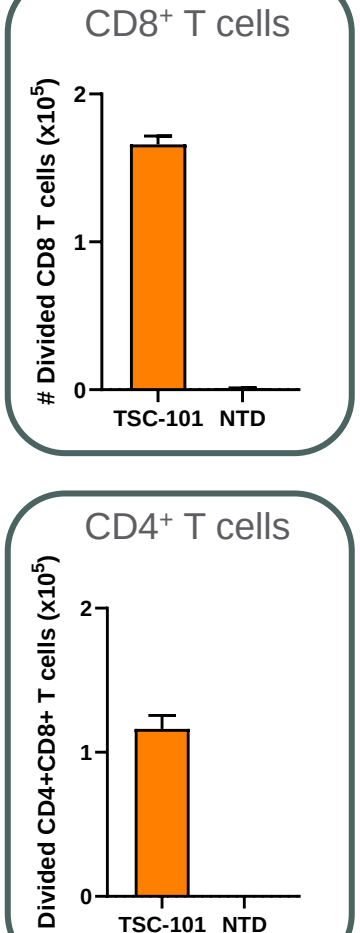
Cytotoxicity



Cytokine production

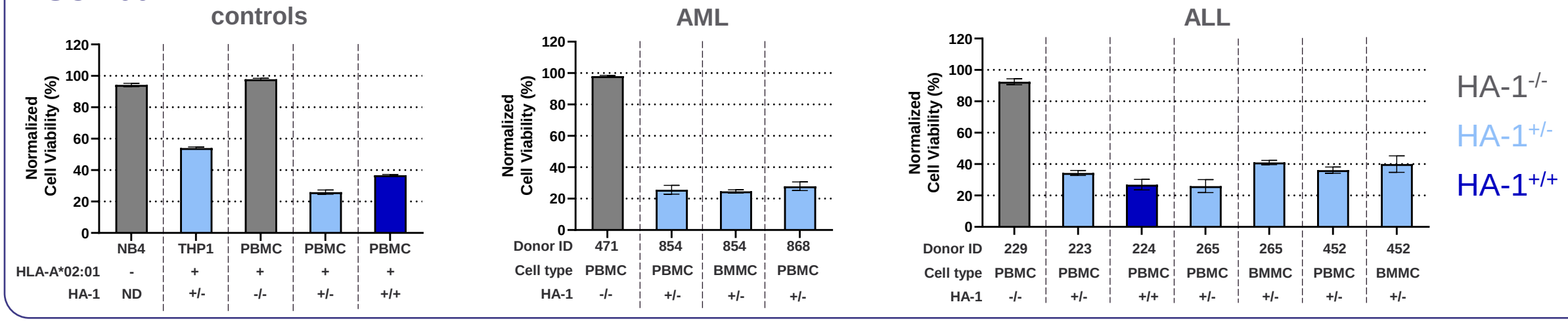


T cell proliferation

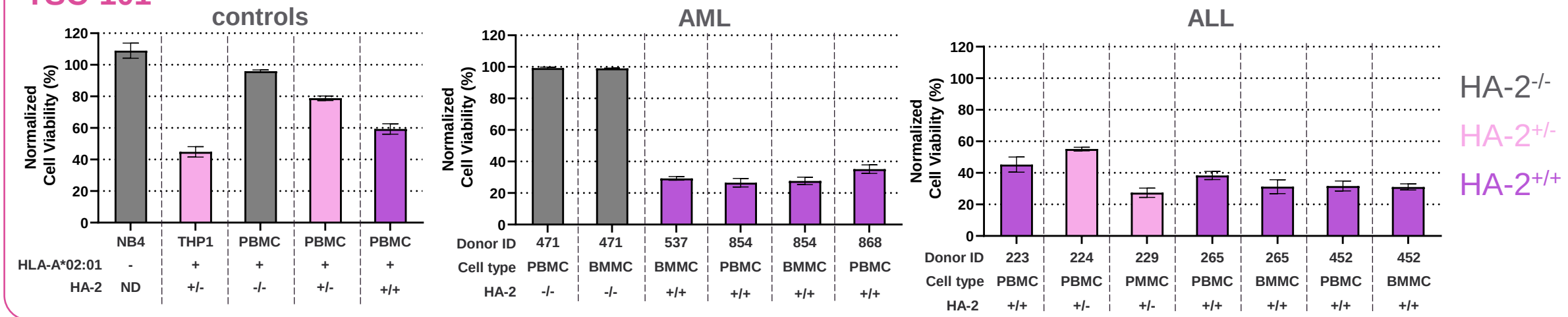


Clinically representative TSC-100 and TSC-101 kill primary tumor specimens (homo- and heterozygous for HA-1 or HA-2)

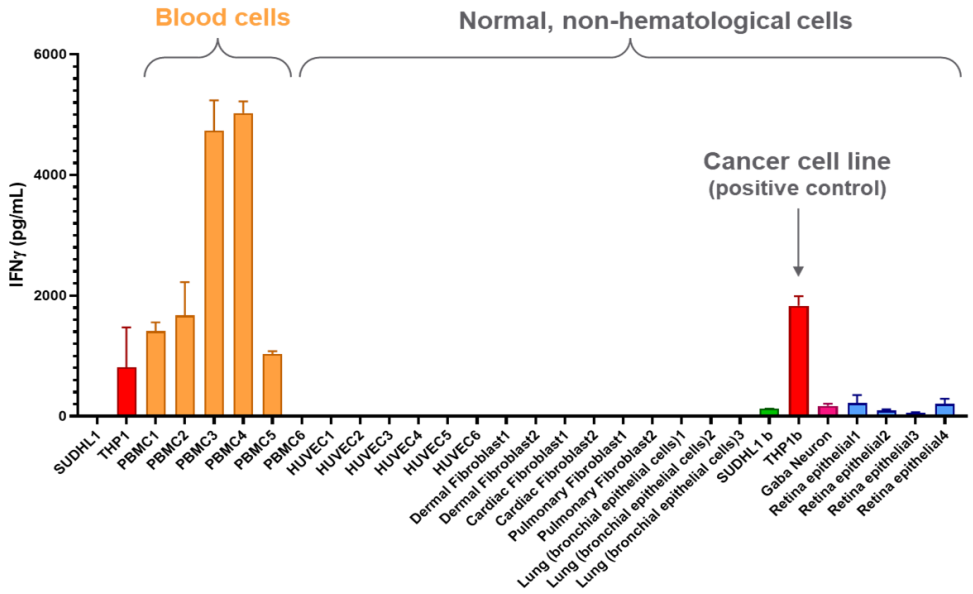
TSC-100



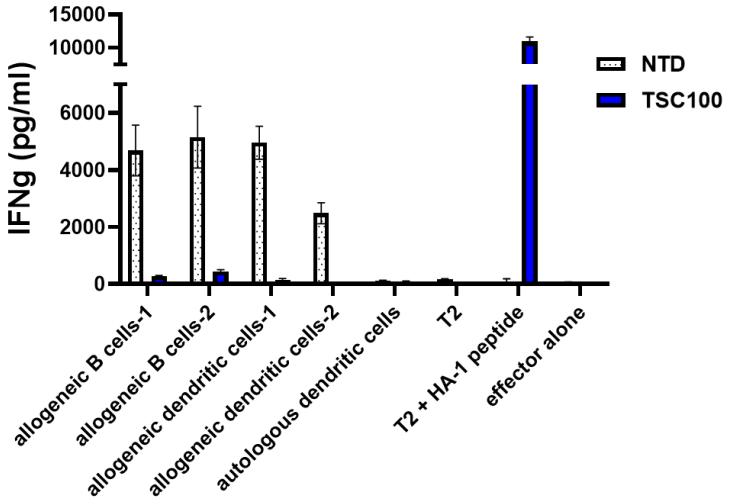
TSC-101



Toxicology studies indicate low risk or off-target toxicity or GvHD



TCR-T cell product recognizes HA-1^{+} hematologic cells but exhibits no recognition of HLA-A*02:01^{+} non-hematologic cells



TSC-100 does not exhibit alloreactivity (indicative of potential GvHD) compared to non-transduced controls

TSC-100 & TSC-101 CLINICAL PROGRAM

Shri Chattopadhyay, M.D.

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

Treatment Type	Patient Genetics	Trial Arm
Treatment arms: **RIC Haploidentical donor transplant** **+ TSC TCR-T therapy**	Patient: **A*02:01+,HA-1+** Donor: **A*02:01+, HA-1- or A*02:01-**	TSC-100 Monotherapy
	Patient: **A*02:01+, HA-2+** Donor: **A*02:01-**	TSC-101 Monotherapy
Control arm: **RIC Haploidentical donor transplant alone**	Patient **A*02:01-** Other HLA types	Standard-of-care

Advantages

- Inclusion of control arm enables comparisons of safety (GvHD) and early efficacy readouts (donor chimerism)
- Same control arm used as comparator
- Maximizes chances of patients receiving active therapy- faster recruitment
- Potential to transition seamlessly to registrational trial (multi-arm, multi-phase) pending regulatory discussions

Retrospective analysis of CIBMTR data supports HLA-based ‘randomization’

1-year outcomes Percentages (CI)	**Disease-free survival**	**Relapses**	**Overall survival**	**Non-relapse mortality**	**Acute GvHD (II-IV) at 6 months**	**Chronic GvHD**
HLA-A*02:01+ (N=444)	52 (48-57)	32 (28-37)	67 (63-72)	15 (12-19)	30 (25-34)	25 (21-30)
Not HLA-A*02:01 (N=864)	50 (47-54)	34 (30-37)	66 (63-70)	16 (14-19)	29 (26-32)	24 (21-28)

Analysis of patients undergoing RIC-HCT from haploidentical donors did not find significant differences in outcomes between patients with HLA-A*02:01 and other HLA types

Endpoints & early readouts of Ph1 TSC-100/101 trial

Endpoints

Primary

- Adverse events compared to SOC
- Dose limiting toxicities
- Patients able to receive multiple doses

Secondary

- Relapse rates at 6m, 1 yr, 2 yrs
- Disease-free survival
- Overall survival

Exploratory

- Kinetics and percentage of donor chimerism by Day 100
- Minimal residual disease rates
- Persistence of TSC-100/101 at Day 100

RIC-haplo relapse rates	HLA-A*02:01 Prob (CI)	Other HLA Prob (CI)
6 months	23 (19-28)%	22 (19-24)%
1 year	32 (28-37)%	34 (30-37)%
2 years	38 (33-44)%	44 (40-48)%

CIBMTR analysis of 1308 patients undergoing reduced-intensity conditioning based haploidentical transplantation from 2017-2019

Early surrogate markers of efficacy in initial dose cohorts

Measurement

Donor chimerism kinetics

Expected Results

Control patients achieve >98% whole blood chimerism at median Day 35 (range 15-170)[1]

TSC-100/101 patients achieve faster and greater CD3 cell chimerism

Measurement

T cell persistence

Expected Results

Sustained persistence of CAR-T cells correlates with anti-leukemia activity[2]

TSC-100/101 patients achieve >3% engineered T cell persistence at Day 100

Measurement

T cell activation

Expected Results

T cell activation at sites of tumors predicts clinical responses[3]

TSC-100/101 cells in bone marrow or blood exhibit activation markers

Measurement

Minimal Residual Disease (MRD)

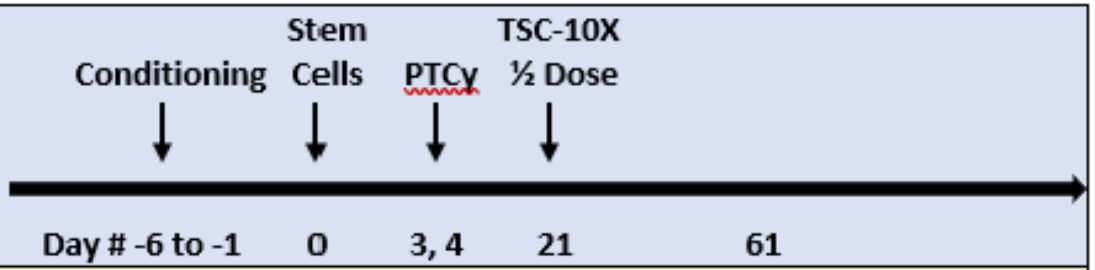
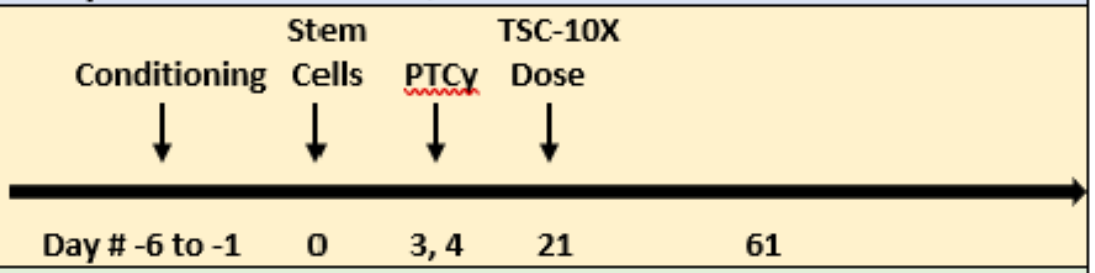
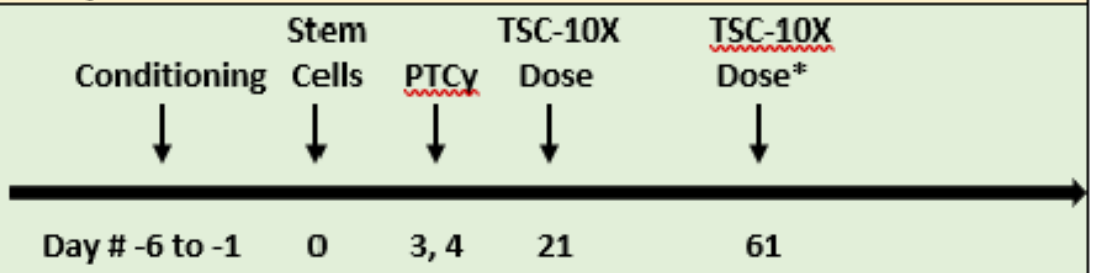
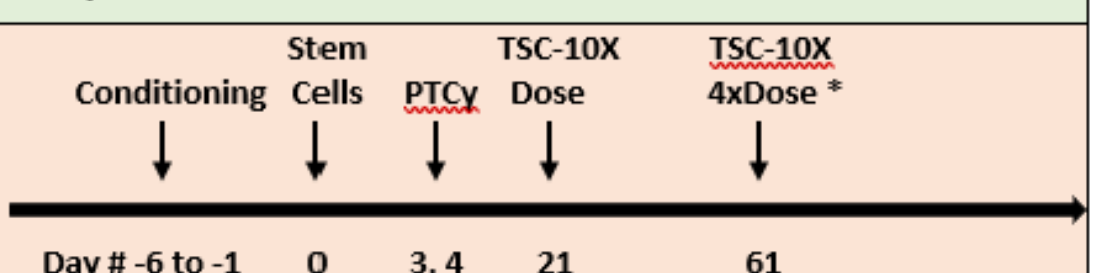
Expected Results

MRD is detected post-transplant by flow in 10-15% of AML patients[4]

TSC-100/101 patients do not have detectable MRD compared with controls

1. https://ashpublications.org/blood/article/128/22/3417/98278/Chimerism-Analysis-after-Haploidentical-Stem-Cell
2. https://www.nejm.org/doi/10.1056/NEJMoa1407222
3. https://insight.jci.org/articles/view/134612
4. https://ashpublications.org/blood/article/119/14/3256/29557/Risk-stratification-directed-donor-lymphocyte

Proposed dose regimen pending regulatory approval

Dose level -1	
Dose level 1	
Dose level 2	
Dose level 3	

Advantages:

1) *Modeled after donor lymphocyte infusion regimens, familiar to BMT clinicians*
2) *Single dose cohort establishes initial safety of products*
3) *Repeat doses adapt to idiosyncratic toxicity. E.g., 2nd dose not given if 1st dose causes GvHD*
4) *Repeat doses increase likelihood of TCR-T cell persistence, minimizing chances of relapse*
5) *Escalating the repeat dose is safer since 1st dose is given soon after HCT when patients are fragile*
6) *May amend protocol in future if needed to administer 3 doses*

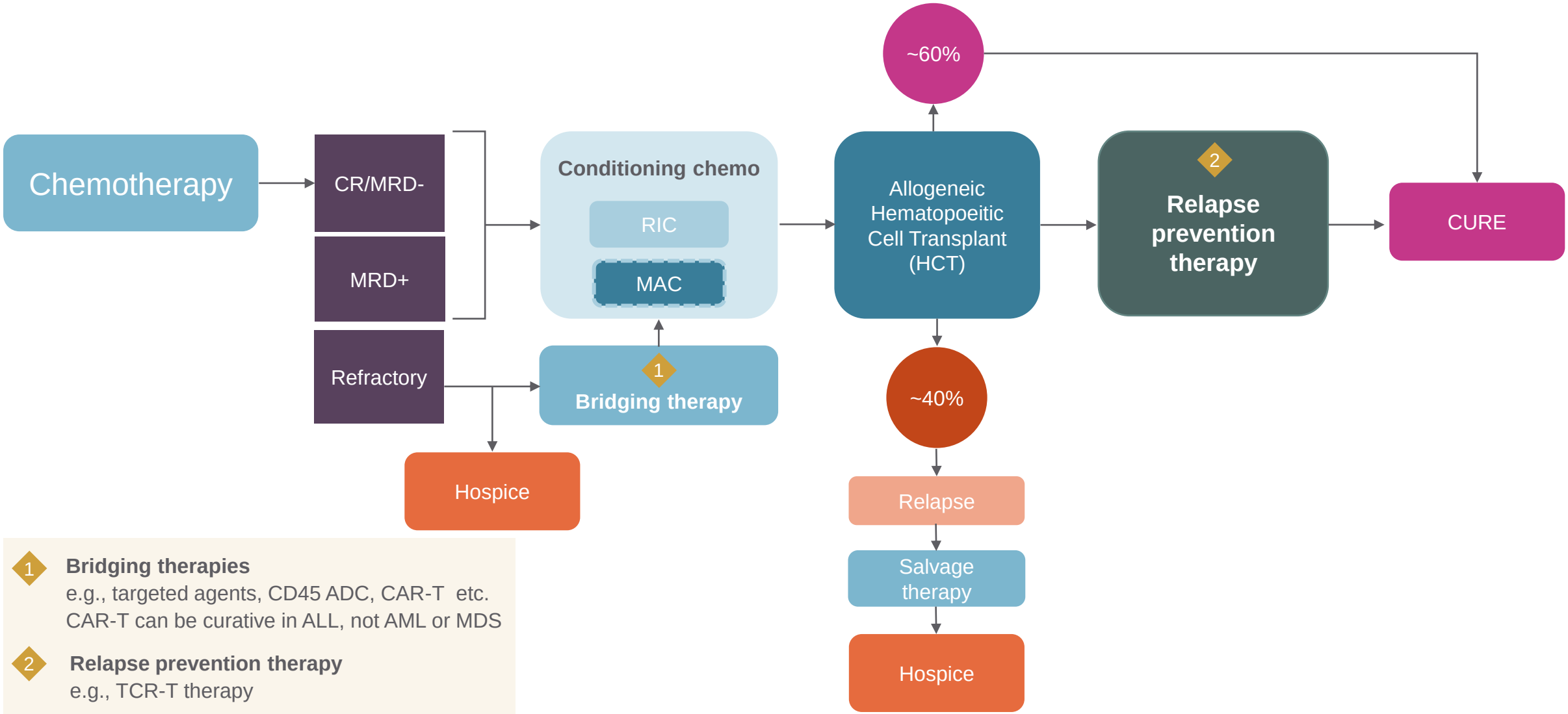
*2nd dose to be administered if no excessive toxicity noted with 1st dose and TSC-10X persistence <3%, after review by the SRC

CLINICAL PRACTICE

Yi-Bin Chen, M.D., M.S.

Massachusetts General Hospital
Harvard Medical School

AML/ MDS/ ALL paradigms—path to cure is through HCT



1 **Bridging therapies**
e.g., targeted agents, CD45 ADC, CAR-T etc.
CAR-T can be curative in ALL, not AML or MDS

2 **Relapse prevention therapy**
e.g., TCR-T therapy

Allogeneic HCT (allo-HCT) transplants are commonly utilized and are the predominant transplant type for AML, MDS, and ALL

HCT Overview

Potential Allogeneic Donor Types

- HLA-Match Related (~25%)
- HLA-Match Unrelated
- Haploidentical

Potential Conditioning Regimens

- Reduced Intensity Conditioning (RIC, ~60%)
- Myeloablative Conditioning (MAC, ~40%)

Source: Lee. Hematologica.2017; Bayraktar. Rev Bras Hematol Hemoter. 2011; UpToDate; HRSA Registry Transplant Activity Report 2013 – 2017; CIBMTR; ClearView Analysis.

[1] Scott et al, J Clin Oncol. 2017 Apr 10;35(11):1154-1161.

HCT Considerations

Overview

- HCT provides eligible patients with a potentially curative solution for select heme malignancies
- Patient age, presence of comorbidities, and functional status determine HCT eligibility

Donor Types

- First donor choice is fully HLA-matched siblings. Next choice between matched unrelated donors (MUD) or haploidentical (haplo) related donors. MUD is more commonly used although haplo has equivalent outcomes

Conditioning

- Conditioning chemotherapy intensity is determined by patient fitness (age, comorbidities, performance status)
- MAC has lower relapse rates (14% vs 48% for RIC) but higher treatment-related mortality (16% vs 4% for RIC)[1]

Prognosis

- Prognosis variable based on heme malignancy, conditioning type, risk category
- The 3-year survival rate (≥ 18 years) following allo-HSCT was ~50% for AML, ~45% for MDS, and ~55% for ALL

Unmet needs in transplant medicine

Preventing relapse is the biggest challenge

- 90% mortality after relapse
- DLI used after relapse but has high risk of GvHD, partial efficacy
- Maintenance therapy trials underway with targeted agents (<20% of patients qualify) or chemotherapy agents like azacytidine
- These studies require prolonged administration requiring ongoing monitoring, risk of cumulative toxicity, poor efficacy

Getting patients to transplant is next challenge

- Patients with advanced age, comorbidities, general frailty are often not referred for transplant
- Patients who do not achieve complete response to chemotherapy often not referred—considered chemo refractory, risk of relapse too high

Time for donor search is a relatively minor challenge

- While matched unrelated donors are preferred at most centers, it can take 2-3 months to identify and get donors ready for transplantation
- Haplo donors (family members) are faster and more motivated to be available at any time

Potential impact of TSC-100/101 success

Lives saved by preventing relapse

Less need for close monitoring after HCT due to lower risk of relapse

Switch of practice to reduced intensity conditioning + TSC-100/101 instead of myeloablative conditioning—less conditioning related mortality and toxicity

Haplo donors used for all HLA-A*02:01 patients instead of matched unrelated donors- faster transplantation

Future clinical trials:

- to further reducing conditioning intensity (e.g., minimal intensity conditioning) combined with TSC-100/101 peri-transplantation potentially extending transplantation to older/ frailer patients
- in patients who do not achieve CR after initial chemotherapy—get more patients into transplantation
- using TSC-100/101 as chemo-free conditioning which is particularly important for non-malignant diseases (e.g., sickle cell anemia)

Q&A