

# Advancing the Allogeneic MAIT Platform for Targeting Solid Tumors

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### Summary

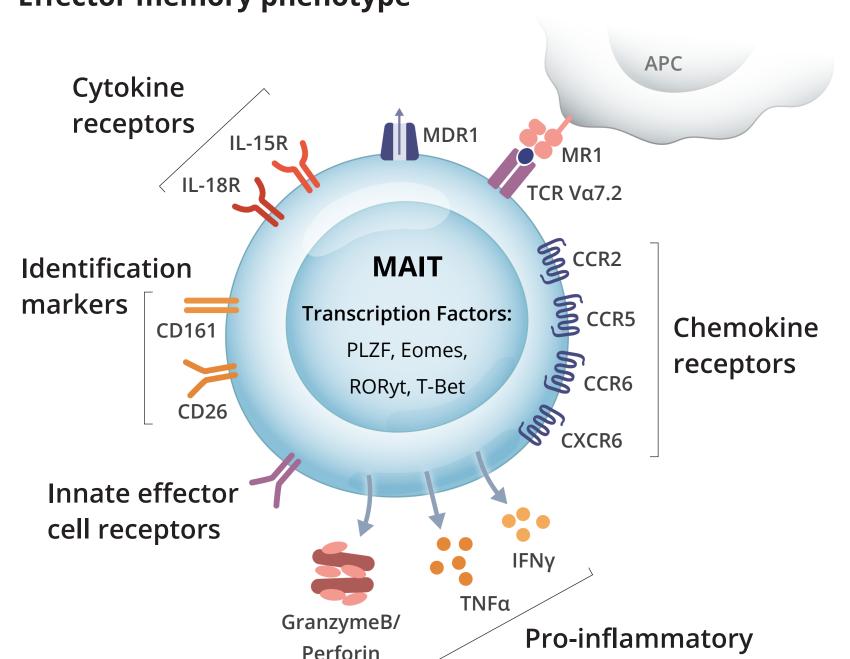
#### Current issues in the field:

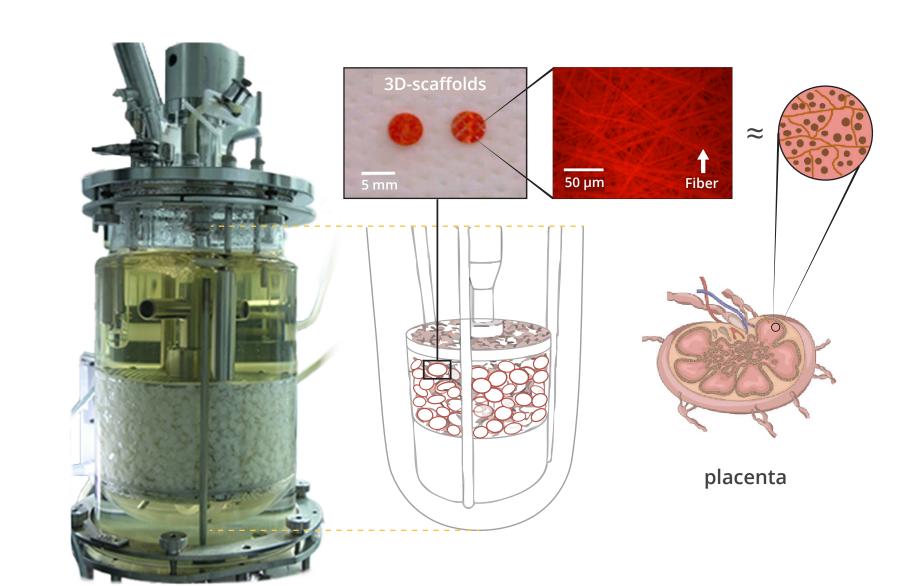
- Recent FDA approvals of the first TCR-T and TIL therapies for solid tumors mark a significant milestone in the field of cell therapy. However, challenges such as low efficacy, inadequate migration to peripheral tumors, and a lack of resistance to tumor counterattacks continue to restrict their widespread application in solid cancers.
- Moreover, transitioning from a patient's own cells to donor cells is the next conceptual barrier, essential for making cell therapy more accessible and affordable.

### Our solution:

- Mucosal-associated invariant T (MAIT) cells are a subset of T cells equipped with unique properties that directly address the major challenges in treating solid tumors.
- Our proprietary 3D platform utilizes porous scaffolds coated with extracellular matrix (ECM) proteins and immune-activating ligands to create a biomimetic microenvironment. This environment closely replicates physiological conditions, optimizing MAIT cell growth. Our system consistently produces a highly functional and proliferative MAIT cell population, generating clinically relevant quantities that surpass those achieved by traditional expansion techniques.
- Our research shows that Pluri's MAIT cells exhibit impressive migratory responses to chemokines and tumor cell line supernatants. Moreover, our CAR-MAIT cells targeting Mesothelin (MSLN) and TCR-MAIT cells specific for NY-ESO-1 have effectively eliminated tumor cells using both 2D and 3D experimental models.

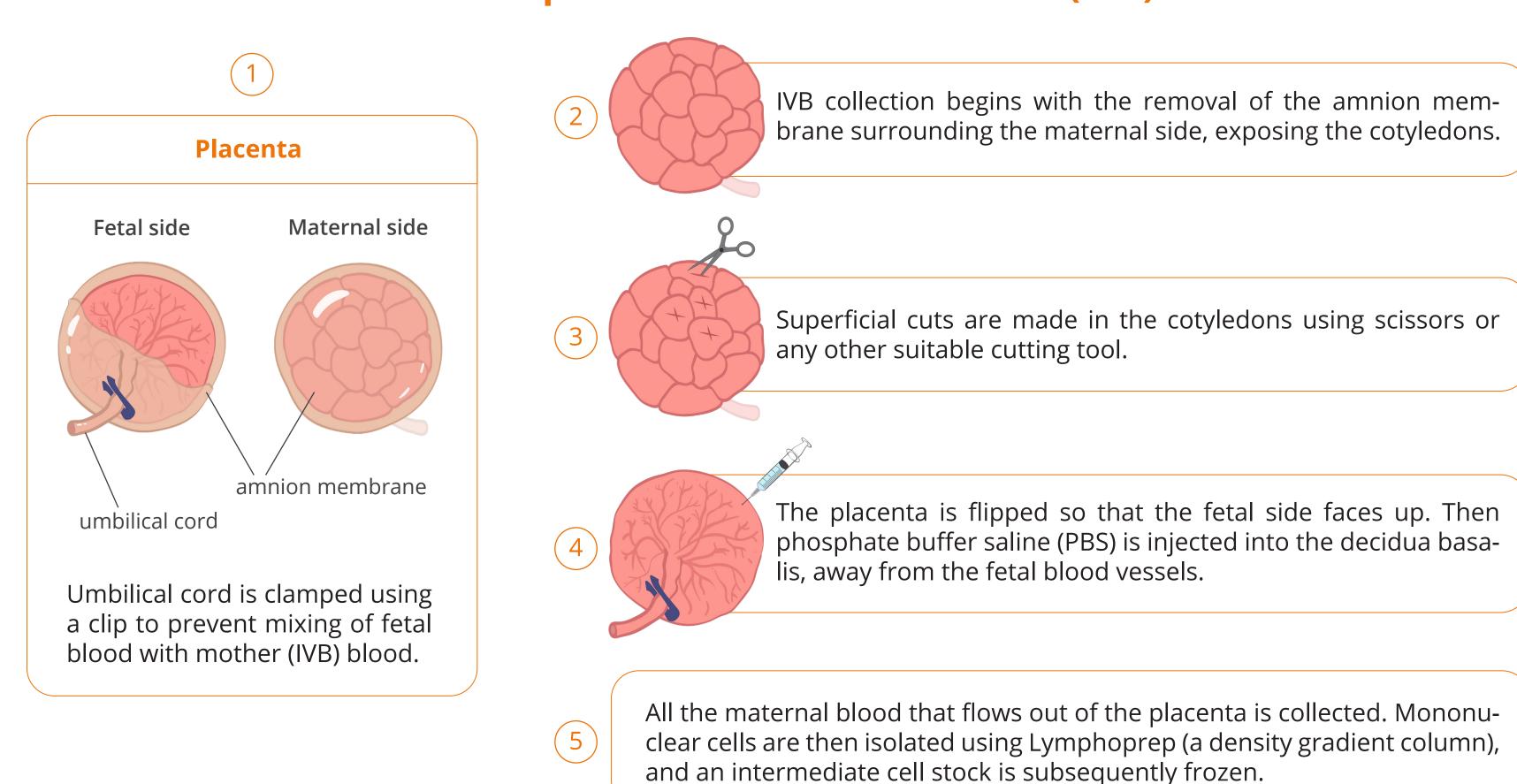
## Effector memory phenotype



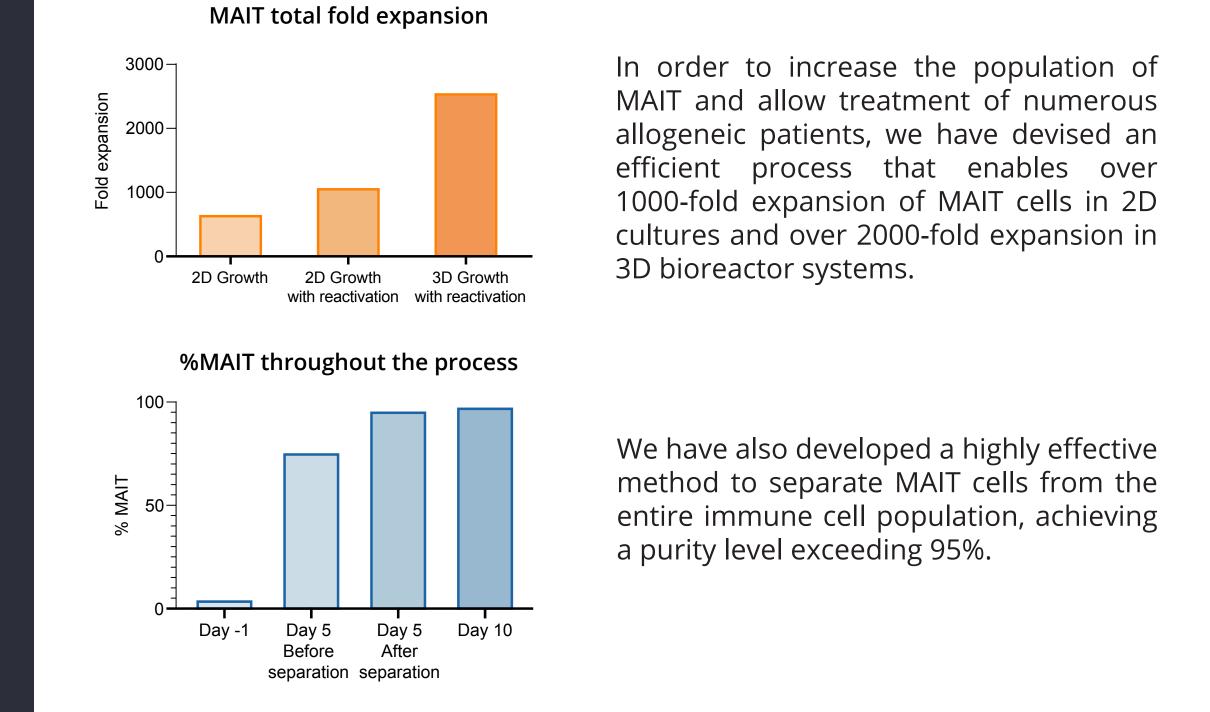


## Methodology & Outcomes

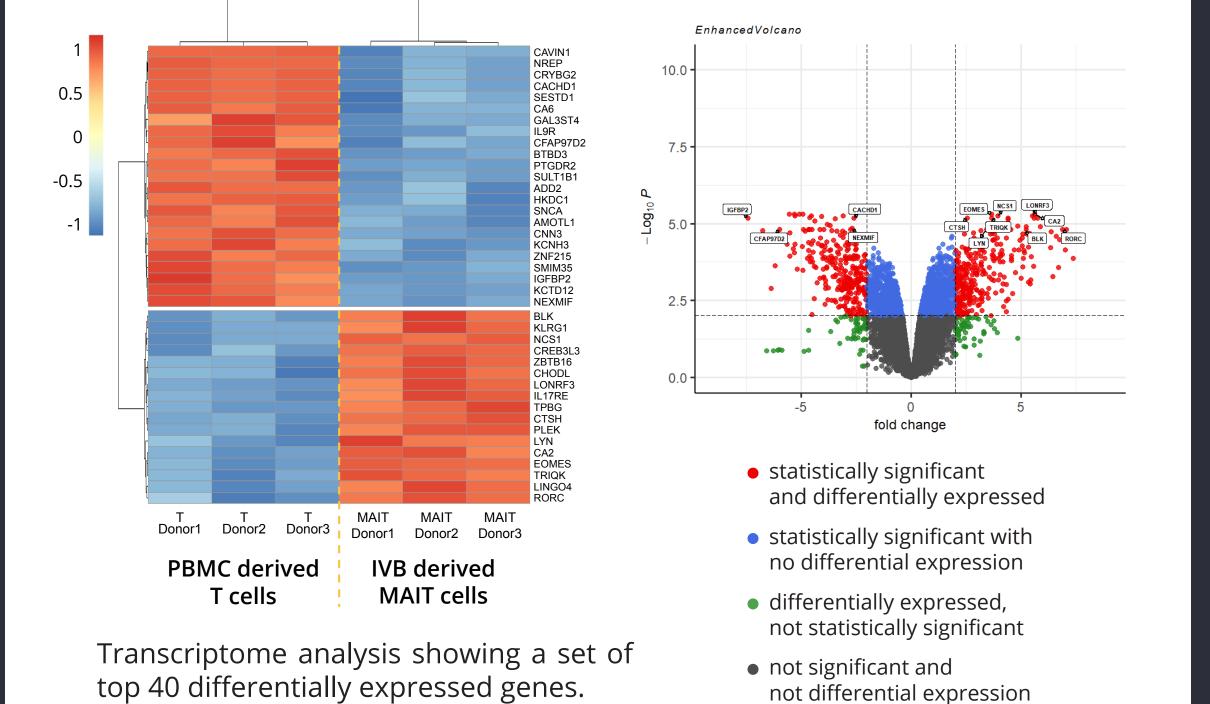
### Isolation of MAIT cells from placental intervillous blood (IVB)



## MAIT expansion and purification process

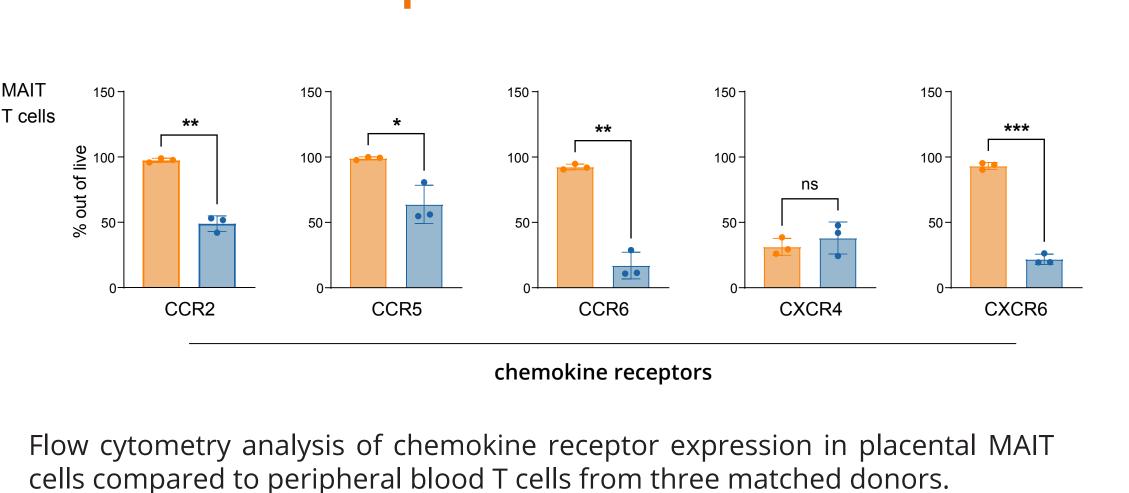


# Placental MAIT cells possess distinct transcriptome pattern compared to peripheral blood T cells



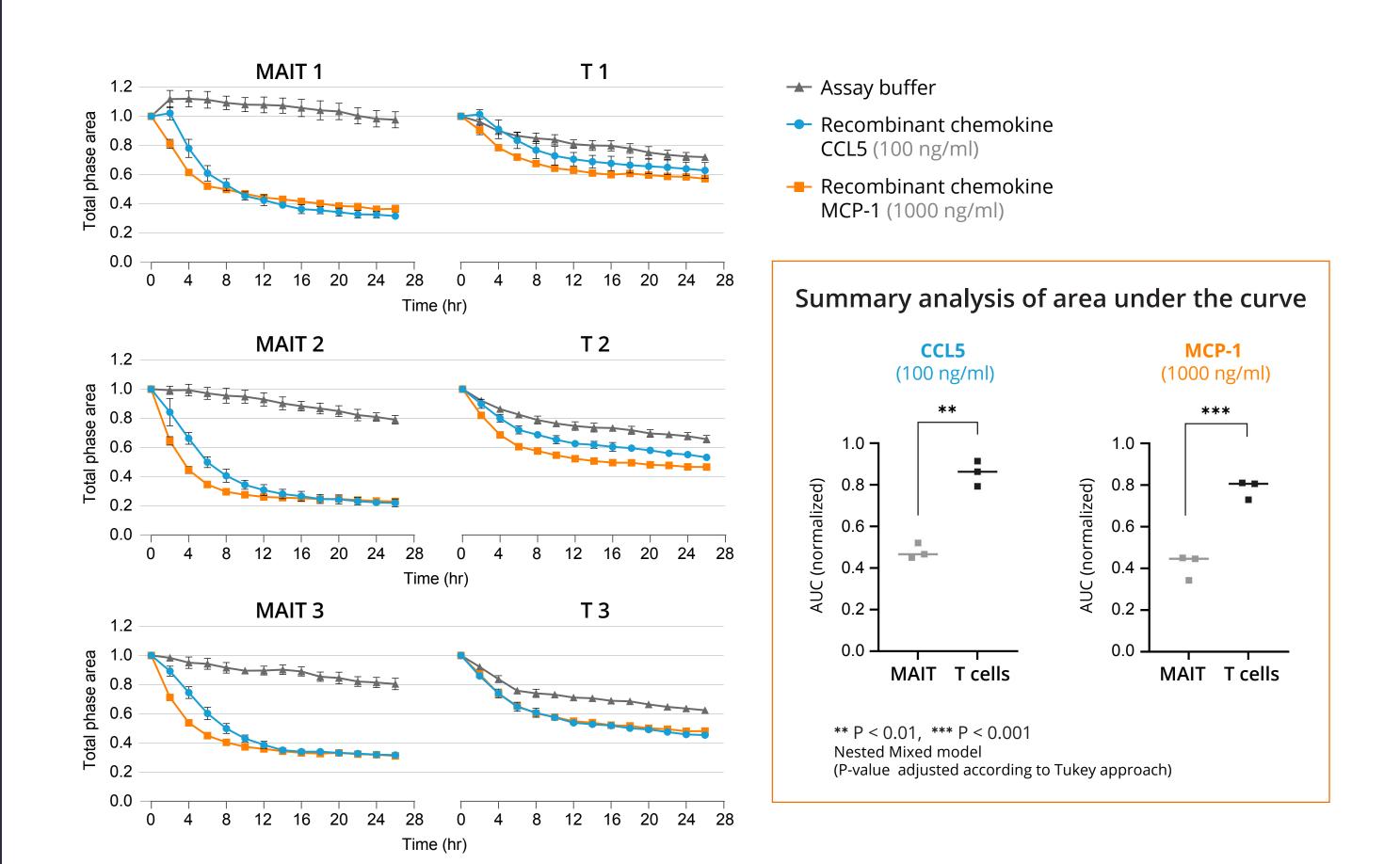
# 4 MAIT cells display high expression of various chemokine receptors

Paired T test. \* P<0.05, \*\* P<0.01, \*\*\*P<0.001



# MAIT cells exhibit superior migratory capacity compared to matched donor T cells

In a real-time chemotaxis assay using the Incucyte imaging system, cells migrate through the pores of a 96-well transwell plate into a reservoir containing chemoattractant. Migration is quantified by measuring the reduction of cells on the upper membrane surface as they pass through the pores.



MAIT cells efficiently migrate toward tumor cell line

Buffer

CL supernatant

NCI-H358

≥ 0.8

Ovarian cancer CL

**OVCAR-8** 

In a real-time chemotaxis assay, placental MAIT cells

demonstrate enhanced migration toward the supernatants

Non-small cell lung cancer CL

NCI-H1703

0 4 8 12 16 20 24 28

Pancreatic cancer CL

of lung, ovarian, and pancreatic cancer cell lines (CLs).

CCL5 at 100ng/ml serves as positive control.

supernatants

<u>\*</u>

0 4 8 12 16 20 24 28

Non-small cell lung cancer CL

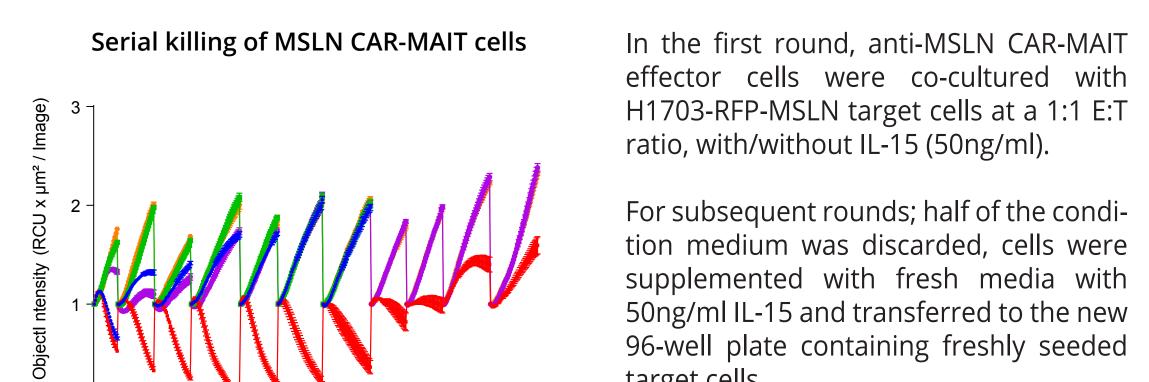
일 0.8

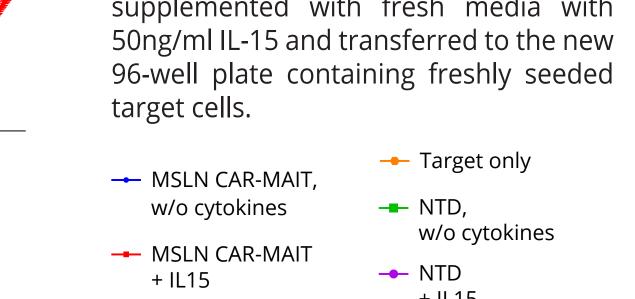
Lung cancer C

≥ 0.8

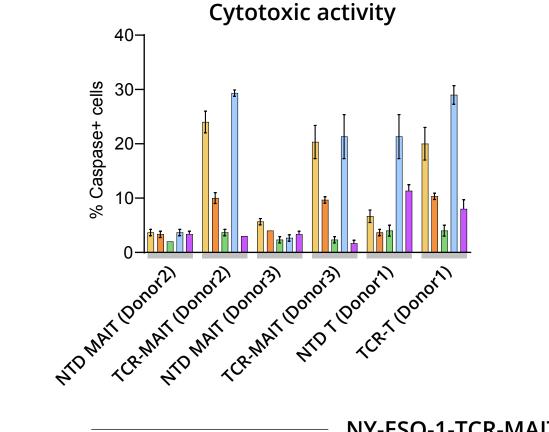
# 8 MSLN-targeted CAR-MAIT cells effectively kill tumor

cells in repeated challenge assays



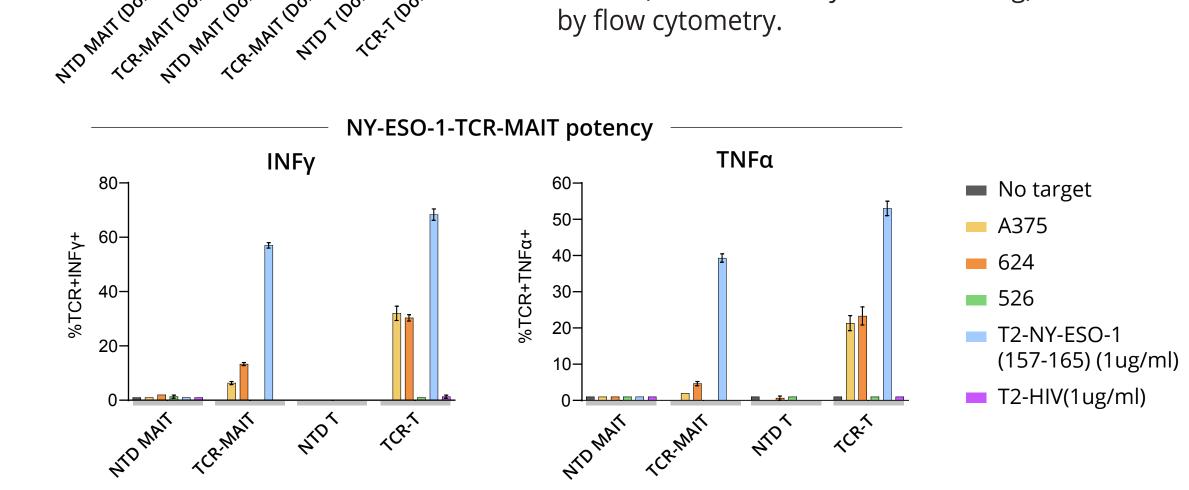




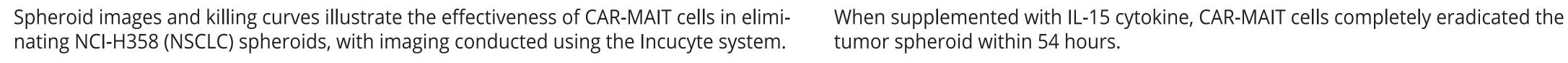


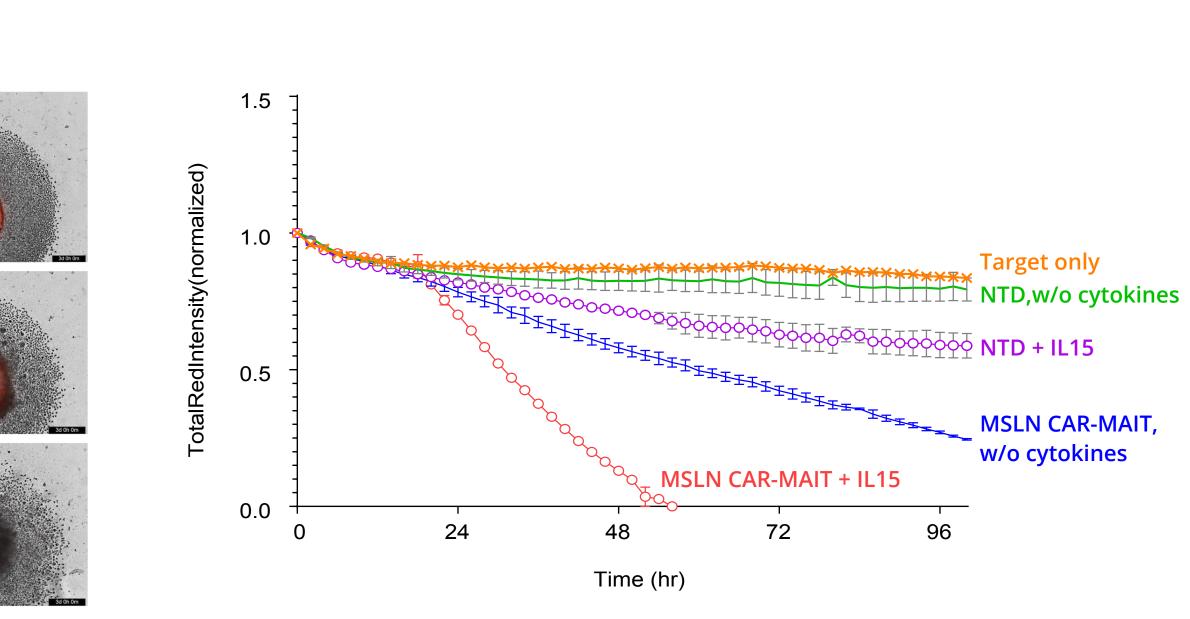
1 2 3 4 5 6 7 8 9 10 1

To test efficacy MAIT and T cells expressing NY-ESO-1 TCR, and the corresponding non-transduced cells, were co-cultured with target cells either expressing NY-ESO-1 (A375, M624, T2 cells loaded with NY-ESO-1 peptide) or negative for NY-ESO-1 (M526, T2 loaded with HIV peptide), at a 1:1 ratio. Efficacy was evaluated by expression of active caspase-3 of target cells (killing) or activation (intra cellular cytokine staining) of T cells by flow cytometry.



# MSLN-targeted CAR-MAIT cells effectively kill tumor cells in 3D spheroid model

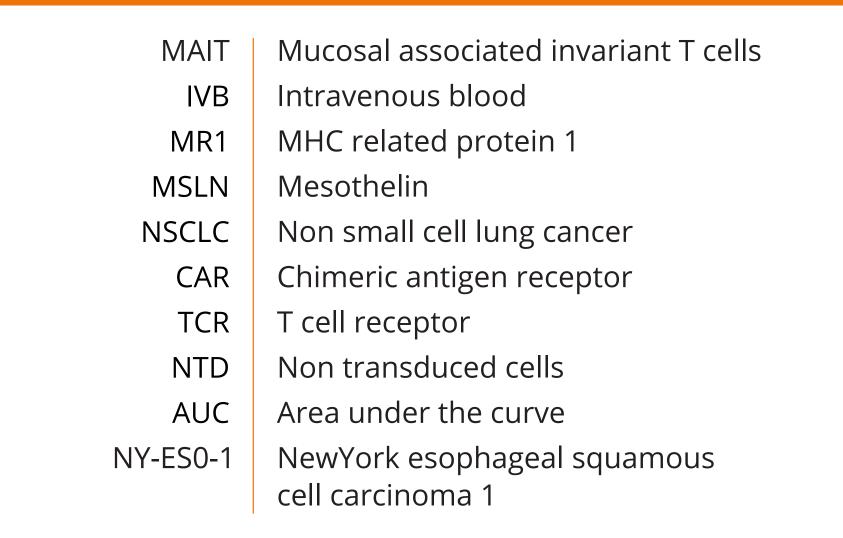




## Conclusions

- Pluri's MAIT cells combine enhanced migration, anti-tumor activity, and functional persistence to overcome key limitations of current therapies.
- Pluri's 3D cell expansion technology enables scalable production of functional MAIT cells for clinical use.
- IVB-derived MAIT cells exhibit distinct characteristics and superior migration compared to PBMC-derived T cells.
- Pluri's MAIT cells demonstrate enhanced migration capacity towards chemokines and supernatant of solid tumor cell lines.
- CAR-MAIT cells targeting MSLN show robust tumor-killing activity.
- TCR-MAIT cells targeting NY-ESO-1 demonstrate strong efficacy against diverse tumors.

## Abbreviations



### Acknowledgem

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