



SENTI BIO

Engineering Smarter Medicines

# Umbilical Cord Blood derived Natural Killer (UCB-NK) Cells Provide a Highly Scalable Source For Gene Circuit-Engineered Allogeneic CAR-NK Therapies

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## ABSTRACT

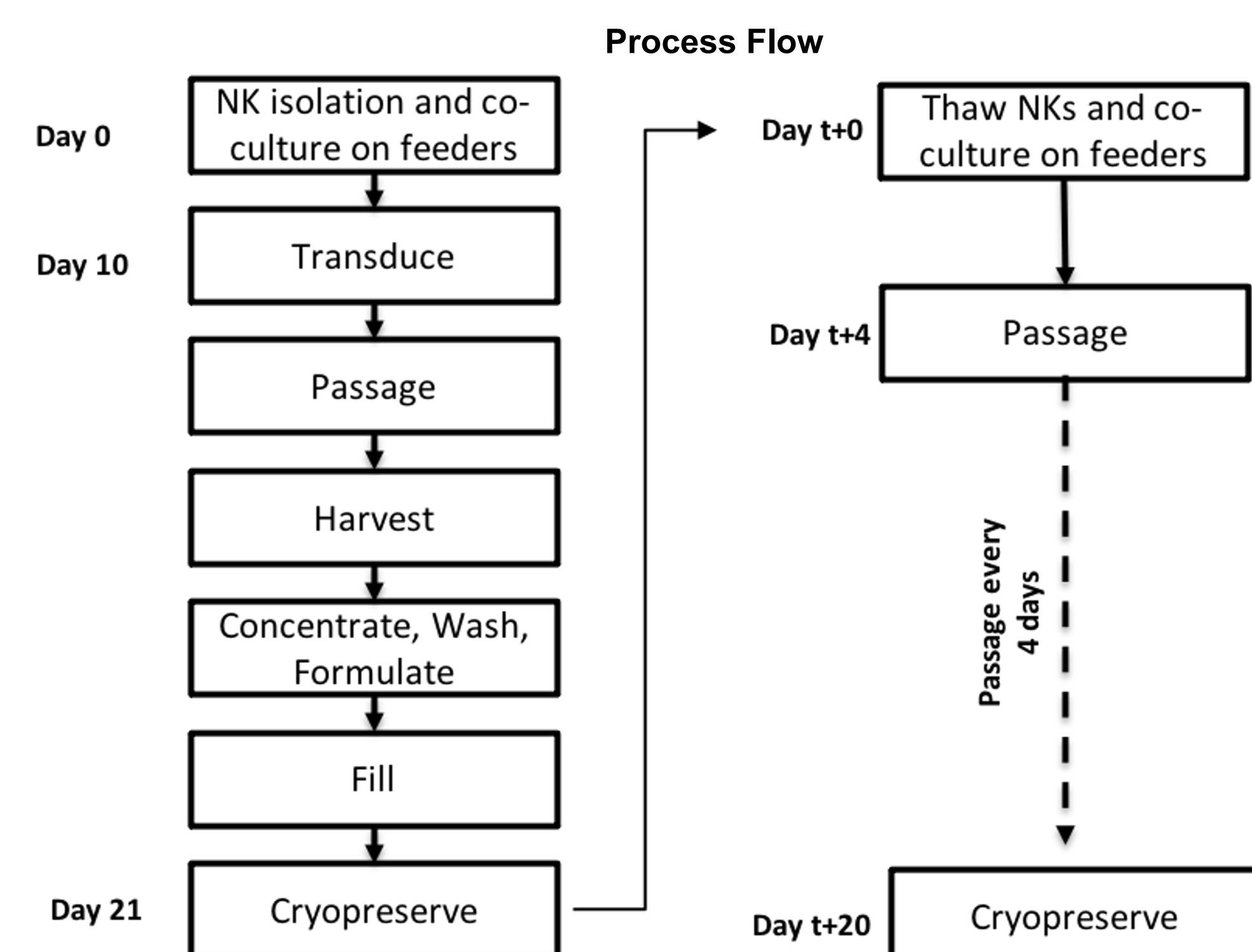
Allogeneic CAR natural killer (NK) cell-based adoptive cell therapy has shown promise in recent years for treating cancer patients. The unique biological properties of Umbilical Cord Blood (UCB) cells along with encouraging results from recent UCB-derived NK cell-based therapies<sup>1</sup> make UCB an attractive source for obtaining large numbers of ‘off-the-shelf’ NK cells. To potentially broaden target tumor types and further enhance anti-tumor efficacy, Senti Bio uses its synthetic biology platform to program ‘gene circuits’ toward engineering optimal efficacy, precision and control into many cell or gene-based medicines, including CAR-NK cells. Here, we studied the transduction efficiency, scalability and cryopreservation of UCB-derived NK cells compared to adult peripheral blood mononuclear cell (PBMC)-derived NK cells in the context of gene circuit-engineered CAR-NK therapy.

## OBJECTIVES

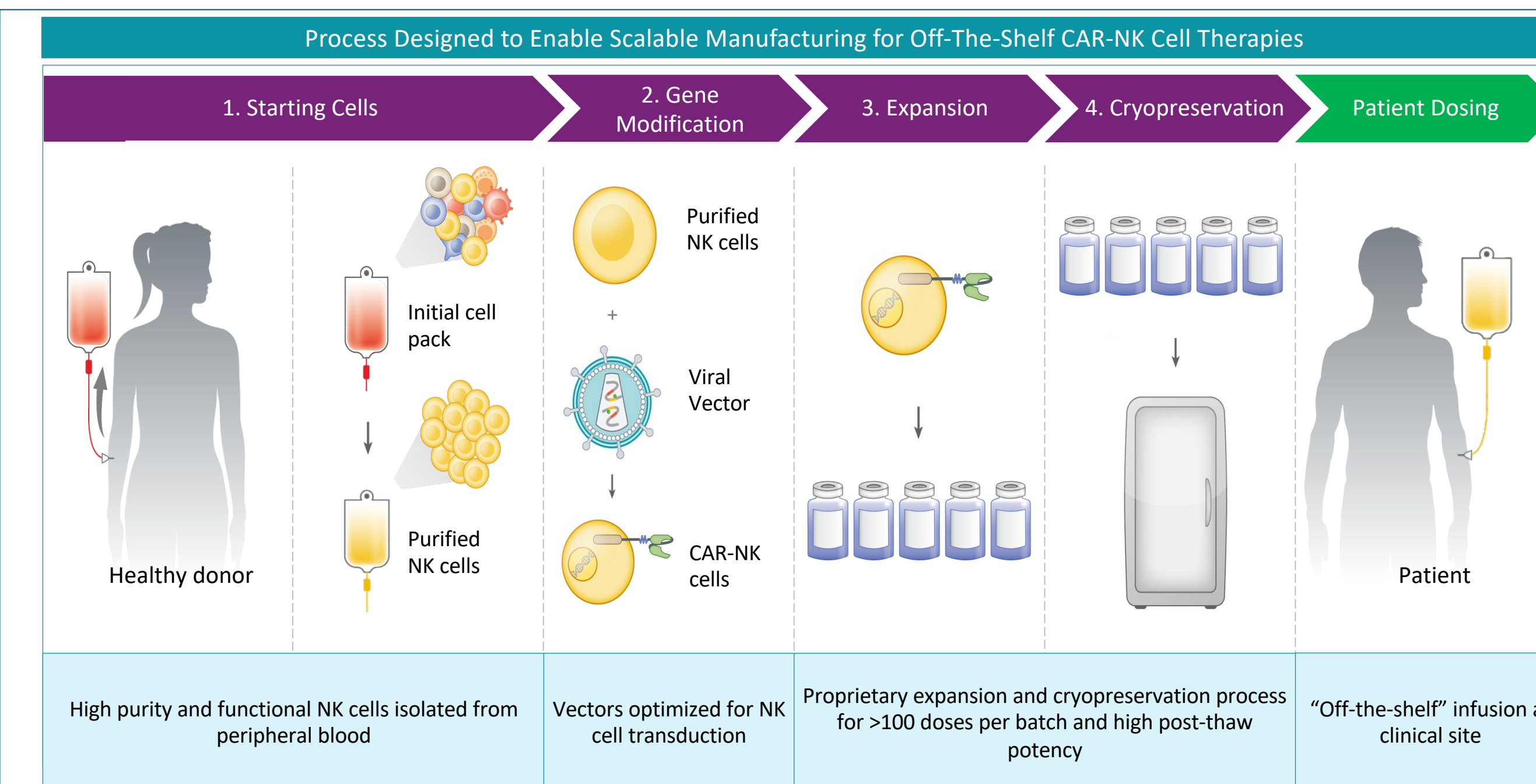
- To evaluate UCB-NK cells as a potential cell source for gene-circuit engineered CAR-NK therapy.
- To compare the expandability, transduction efficiency and functionality of UCB-NK cells and PBMC-NK cells.

## METHODS

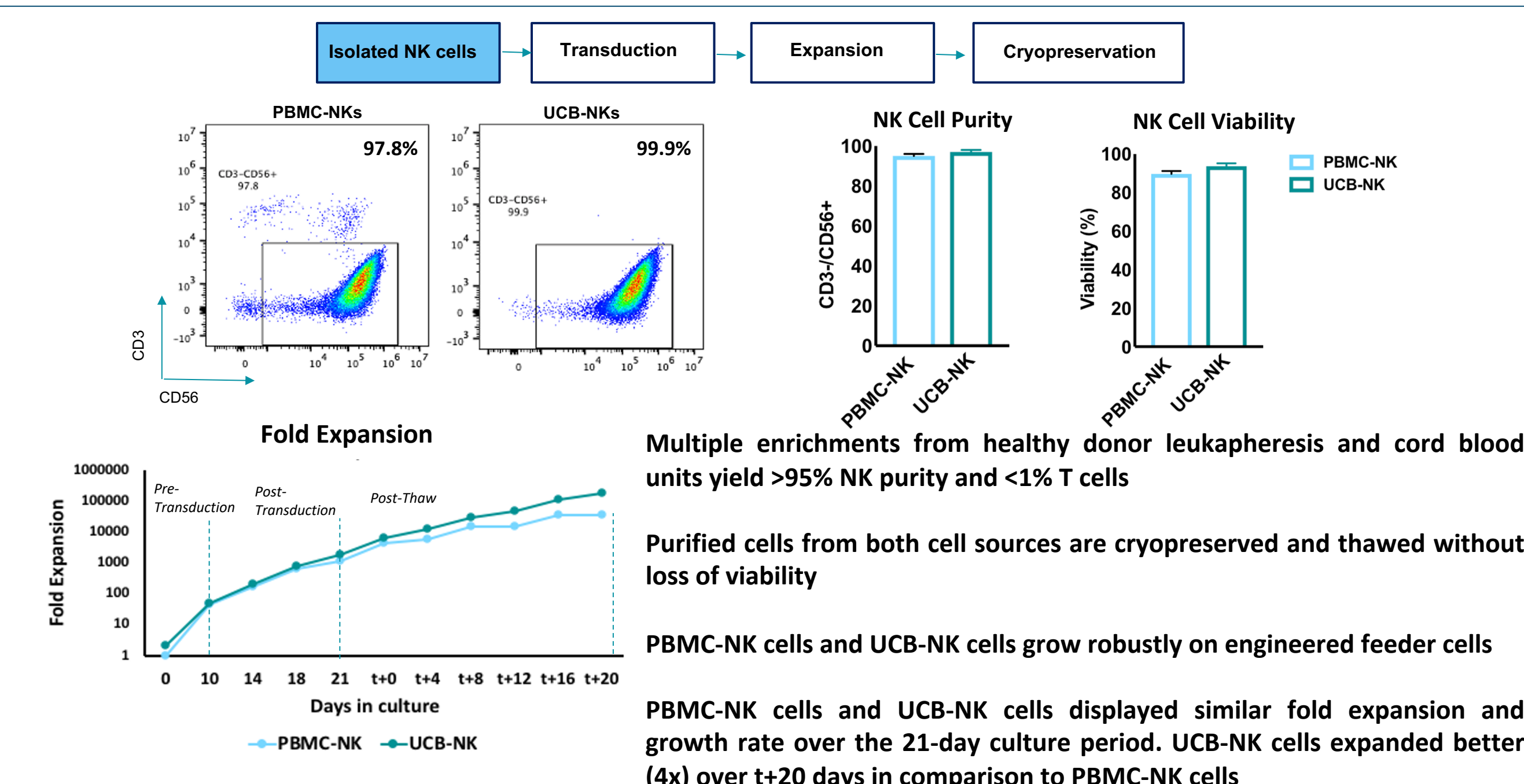
- NK cells were isolated from UCB units and peripheral blood leukapheresis following CD3 depletion and CD56 selection.
- Isolated NK cells were expanded on irradiated gene-modified feeder cells and transduced with GFP- and CAR-expressing constructs.
- Gene-modified NK cells were cryopreserved post-transduction and further expanded post-thaw.



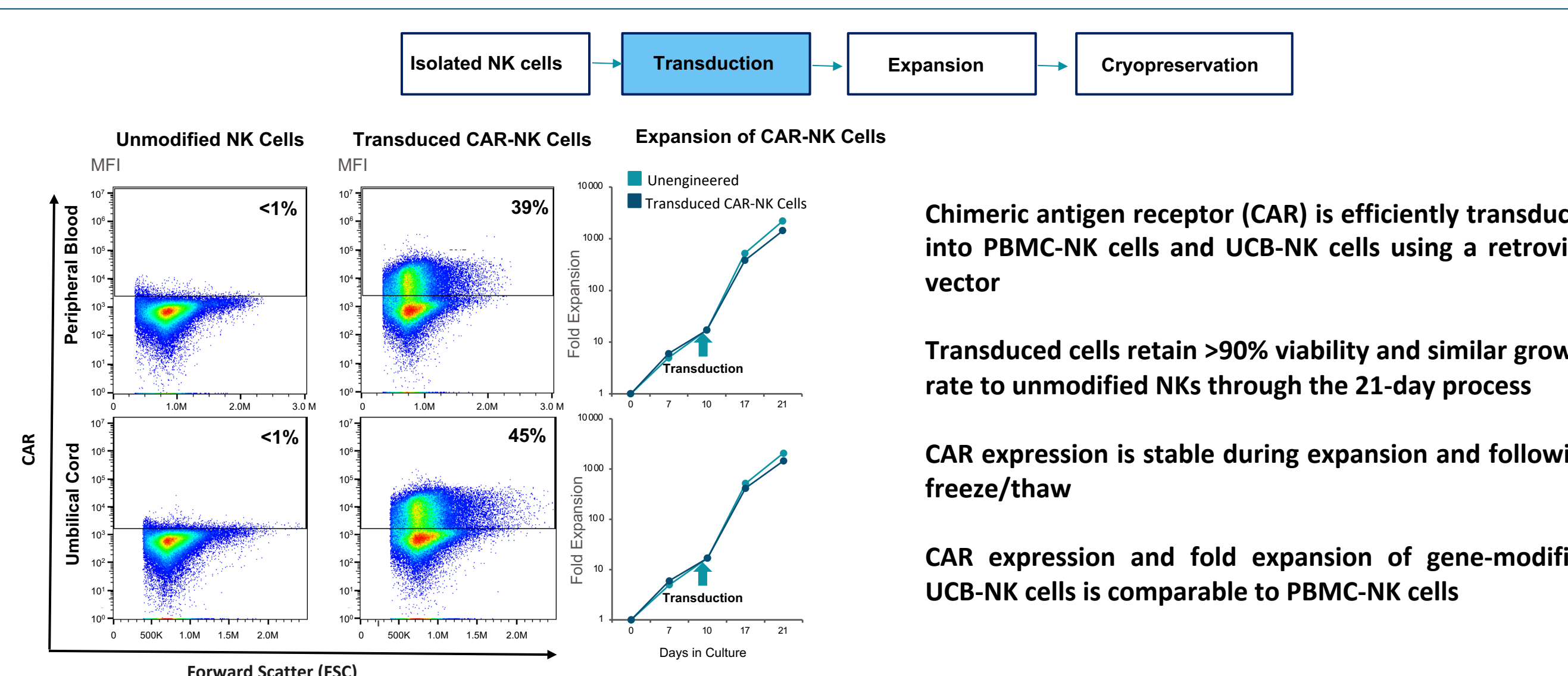
## Senti’s Allogeneic NK Cell Process is Designed to Enable Scalable Manufacturing for Off-The-Shelf NK Cell Therapies



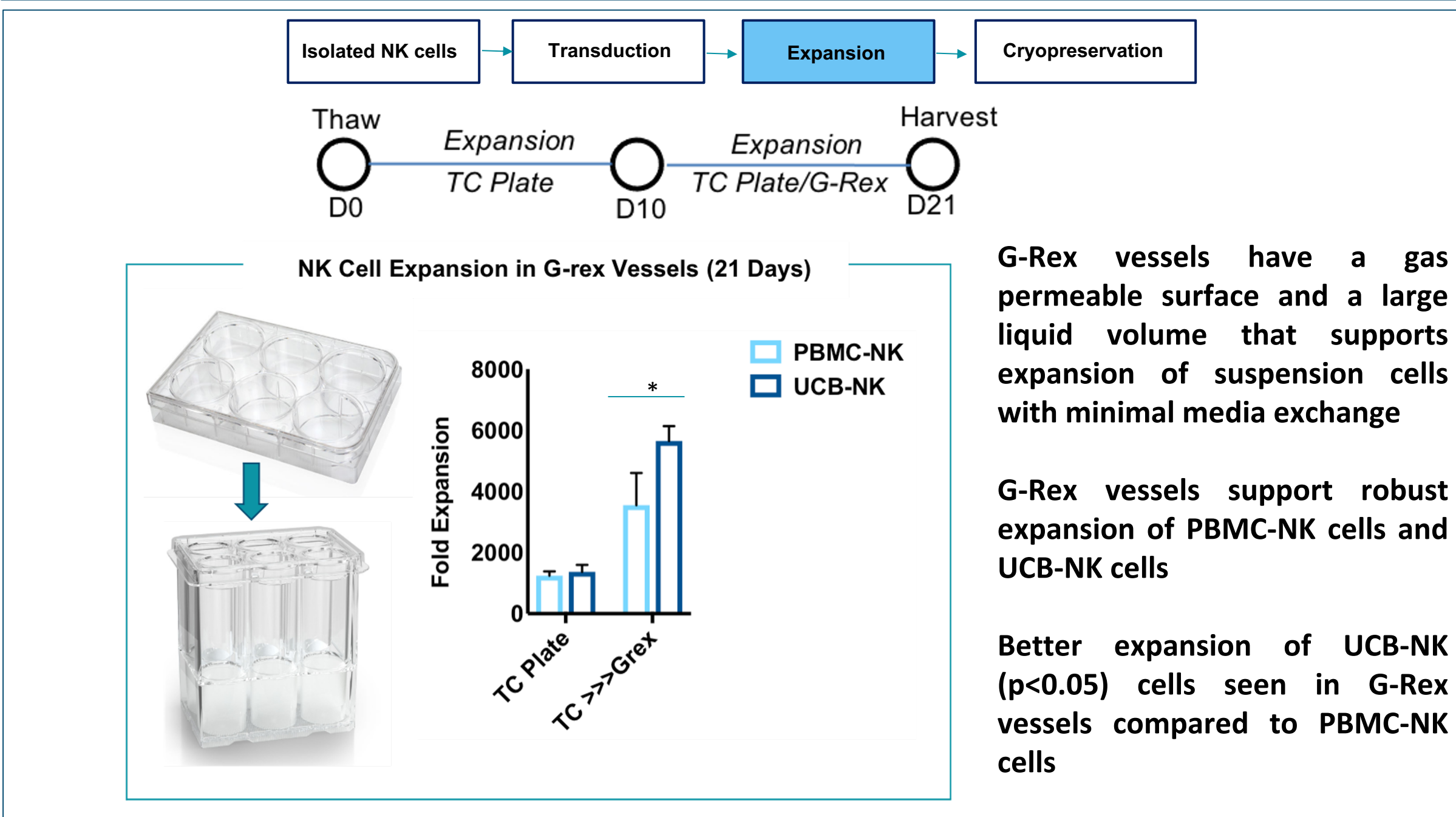
## Enrichment of NK cells from Adult Peripheral Blood and Umbilical Cord Blood Units



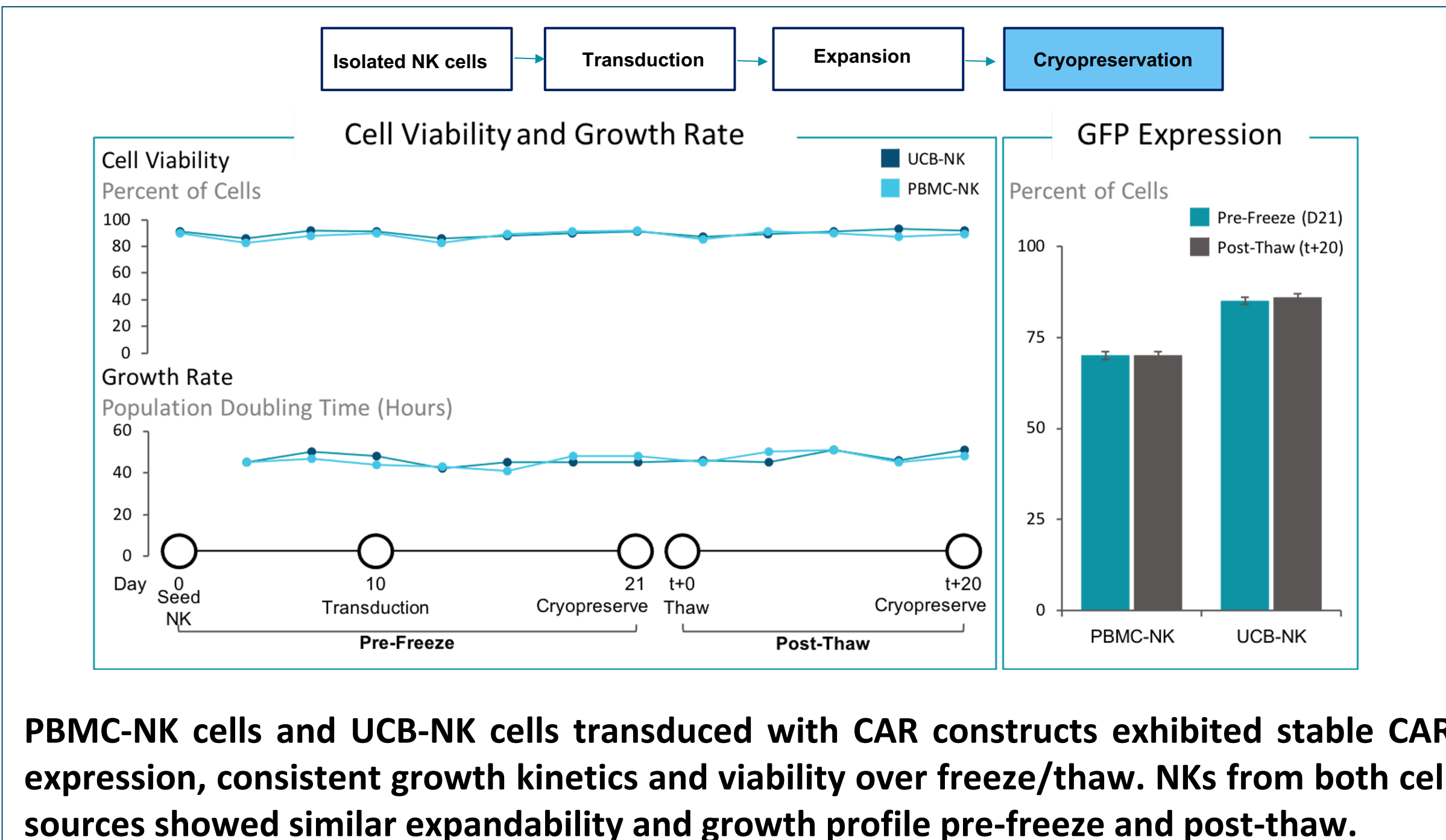
## We Believe Transduction Enables Robust Expression of Gene Circuits



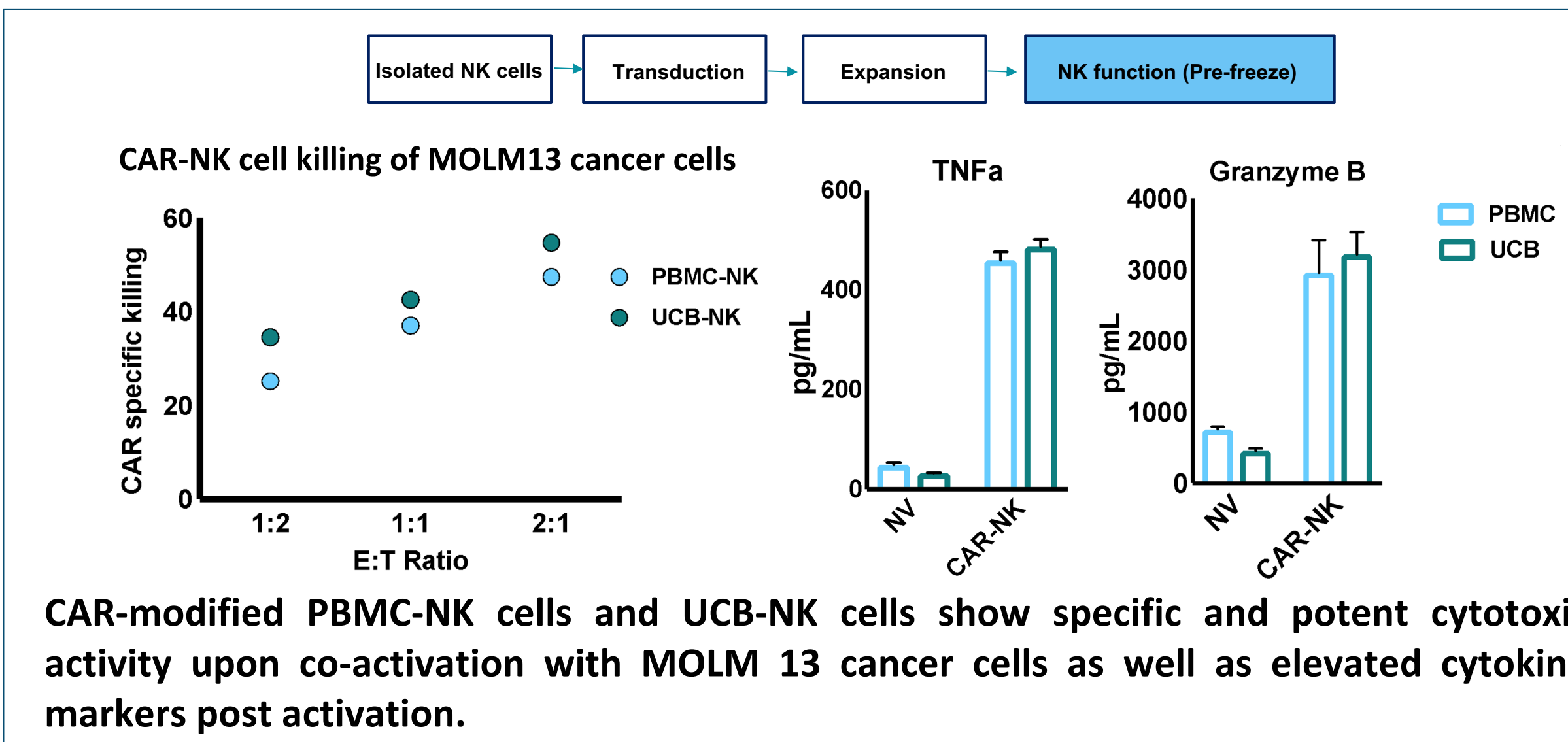
## Robust Expansion of NK cells using GMP-compatible G-Rex Vessels



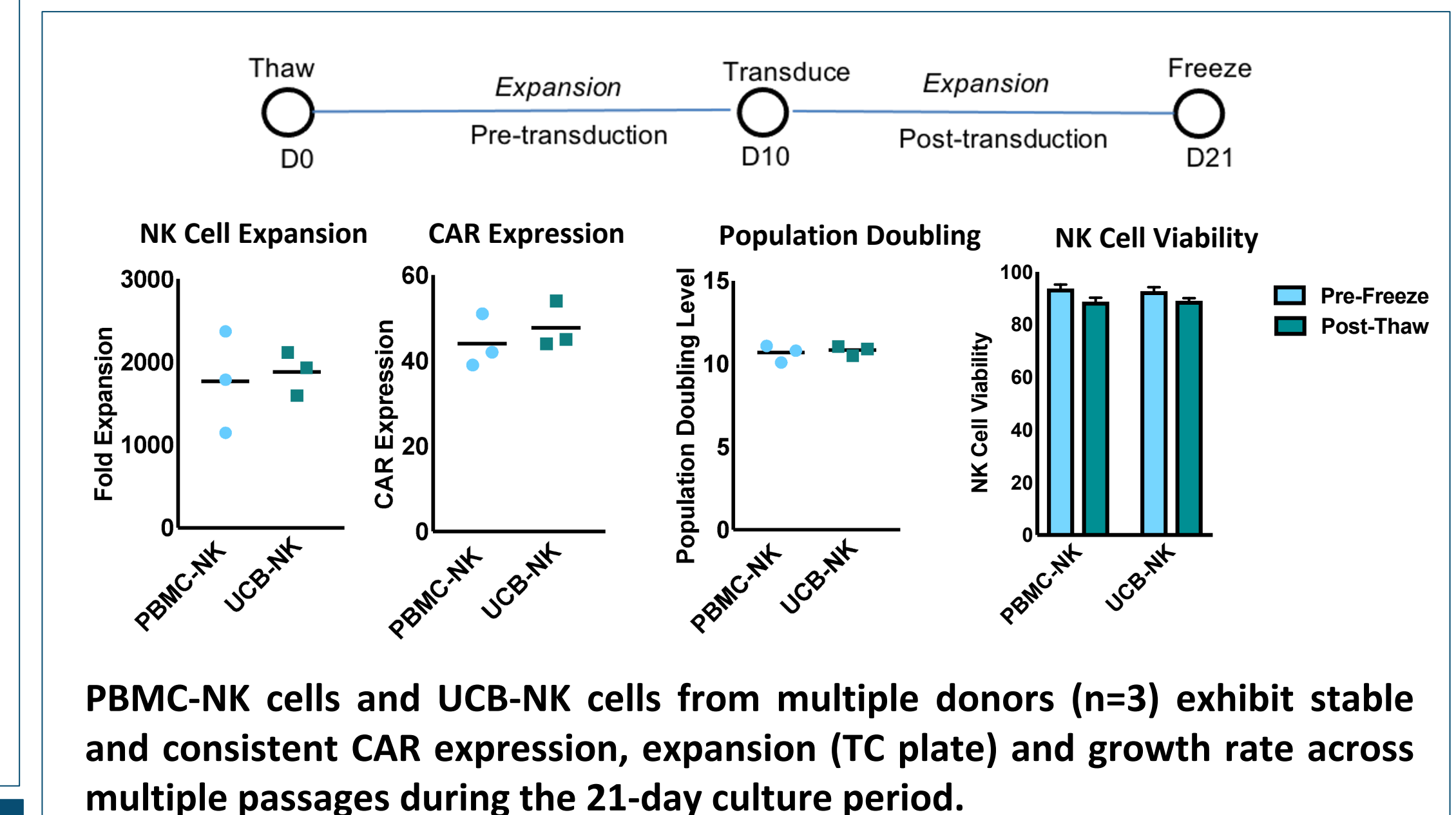
## Cryopreserved NK cells Retain Expandability and Gene Expression Post-Thaw



## Cryopreserved NK cells Retain Expandability and Gene Expression Post-Thaw



## Process Supports Consistent Expansion, Activation and Stable CAR Expression in NK cells from Multiple Donors



## SUMMARY

Achieved highly efficient retroviral vector mediated transduction of allogeneic UCB-derived NK cells through transduction optimization studies

Process yielded consistent growth rate of gene modified CAR-NK cells and stable transgene expression between freeze/thaw

Product attributes were comparable between PBMC-NK cells and UCB-NK cells and across multiple donors

Gene-modified CAR-NK cells show potent anti-tumor activity against target cancer cells in an *in vitro* cell-based cytotoxicity assay

Large scale expansion of UCB-NK cells and PBMC-NK cells provide a scalable source for gene circuit-engineered allogeneic CAR-NK therapies

## REFERENCES

1. Liu E, Marin D, Banerjee P, et al. Use of CAR-transduced natural killer cells in CD19-positive lymphoid tumors. *N Engl J Med*. 2020;382(6):545-553. doi: 10.1056/NEJMoa1910607