

Long-term Stability of iPSC-Derived CD34+ Cell Banks Supports the Sustainable Manufacture of Off-the-shelf Immunotherapies



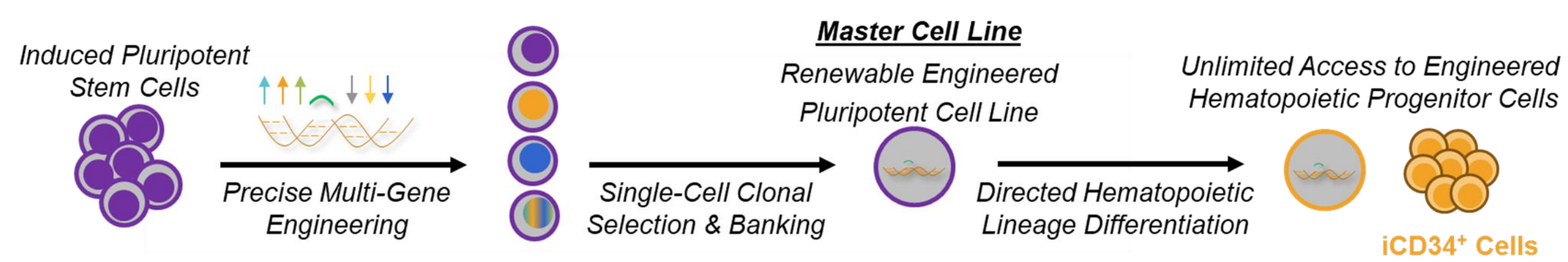
Antonio Fernandez-Perez, Karina Palomares, Christine Chen, Krystle Yakshe, Hui Ding, Chris Lynn, Svetlana Gaidarova, Xu Yuan, Raedun Clarke and Bahram Valamehr
 Fate Therapeutics Inc, San Diego, CA, USA Correspondences: bob.valamehr@fatetherapeutics.com

ABSTRACT & INTRODUCTION

Human induced pluripotent stem cells (hiPSC) have the unique dual properties of unlimited self-renewal and differentiation capacity into all three somatic cell lineages. To further leverage these attributes, we have established a versatile iPSC product platform that enables multiplexed engineering of hiPSCs at the single-cell level and have developed a proprietary differentiation protocol to support definitive hematopoiesis for the derivation of CD34+ hematopoietic progenitor (iCD34) cells. We have shown that these iCD34 cells exhibit multilineage differentiation to diverse subsets of immune cells, including Natural Killer (NK) and $\alpha\beta$ T cells. The highly efficient and scalable differentiation platform is chemically-defined and cGMP-compatible, and iCD34 cells can be cryopreserved, banked and stored. Here we show the successful cryopreservation and long-term cryogenic storage of iCD34 cells, as well as the ability of these long-term stored iCD34 cells to serve as an intermediate feedstock for mass production of iPSC-derived NK and T (iNK and iT, respectively) cell therapies

iPSC Product Platform

Disruptive Approach Enabling Mass Production of Universal NK Cell and T-Cell Products



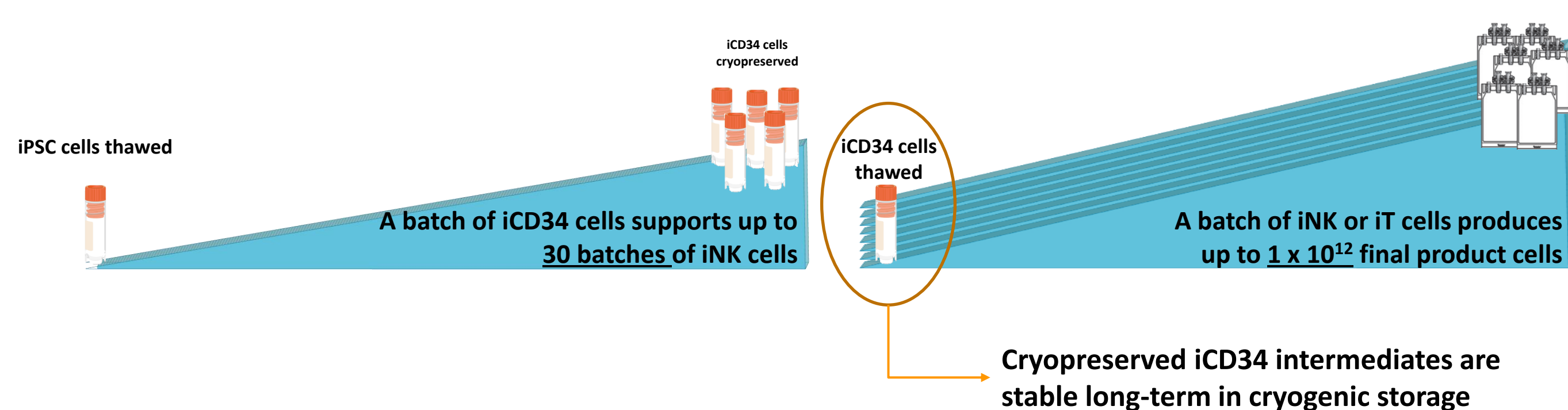
Off-the-Shelf | Homogeneous | Cell Products

Does not require patient-sourced cells Off-the-shelf production of cells
 Consistent and reliable product forms Unprecedented scalability Cost-effective

Addresses Critical Limitations of Patient-Sourced Cellular Therapies

SUMMARY

Stage 1: iCD34 Cell Production Stage 2: NK or T Cell Production

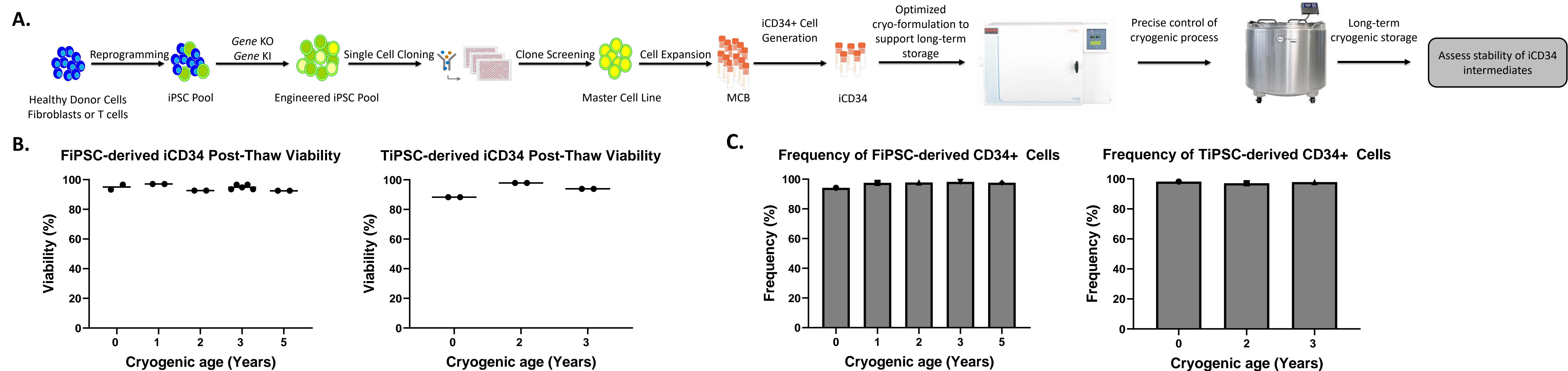


This study demonstrates that manufactured, cryopreserved, and stored iCD34 cells are stable over long-term storage and serve as a robust starting material for mass production of iPSC-derived cell-based immunotherapies.

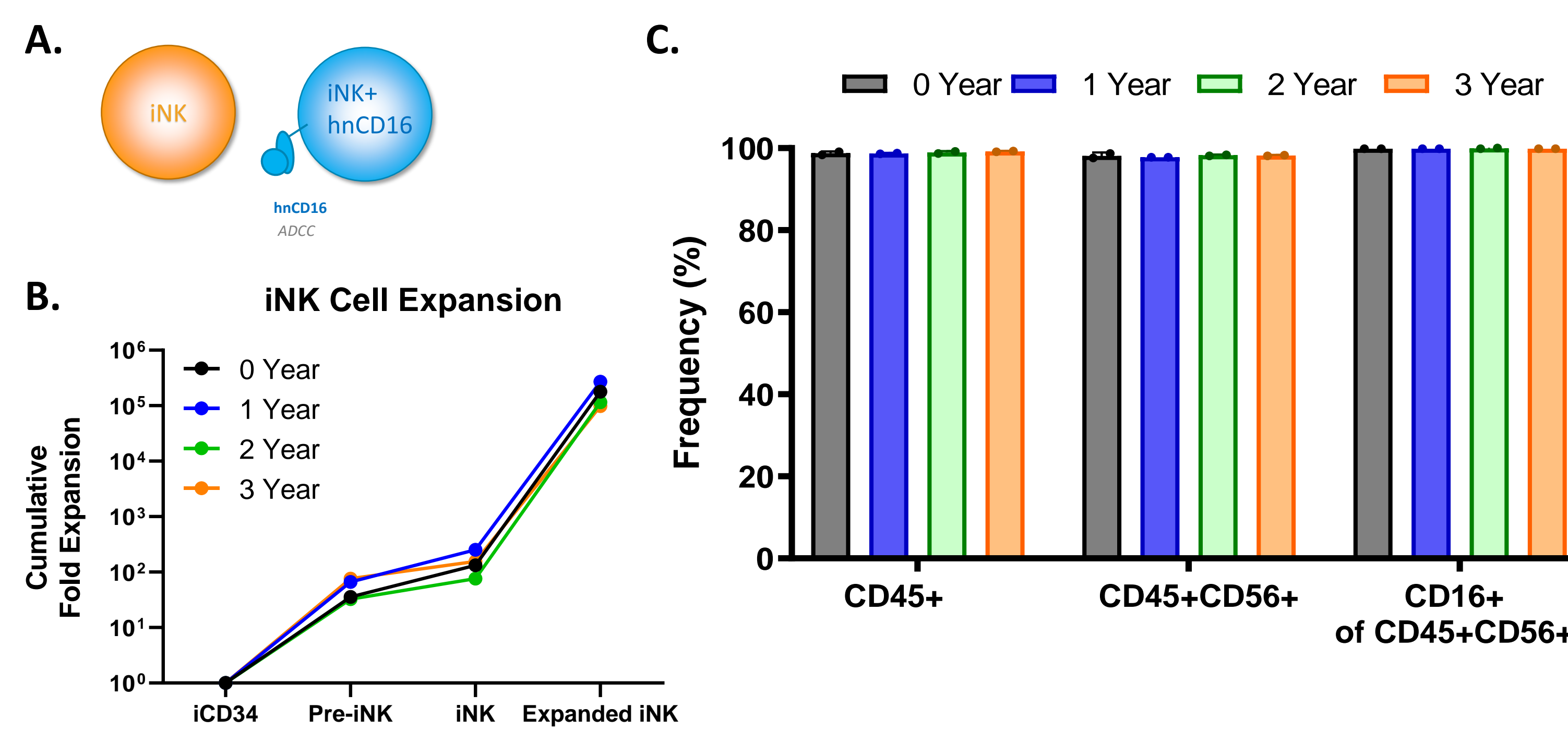
- Long-term stored iCD34 cells demonstrated minimal change of cell health per viability (<10%) upon thaw and showed consistent cell identity and purity
- Long-term stored iCD34 cells maintained full differentiation potential, supporting scaled expansion and uniformity of the final iNK and iT cell product.
- The manufactured iNK and iT cells exhibited high expression of engineered modalities and maintained robust potency as demonstrated by cytokine release and in vitro target cell killing assays. Additional tests are ongoing.

RESULTS

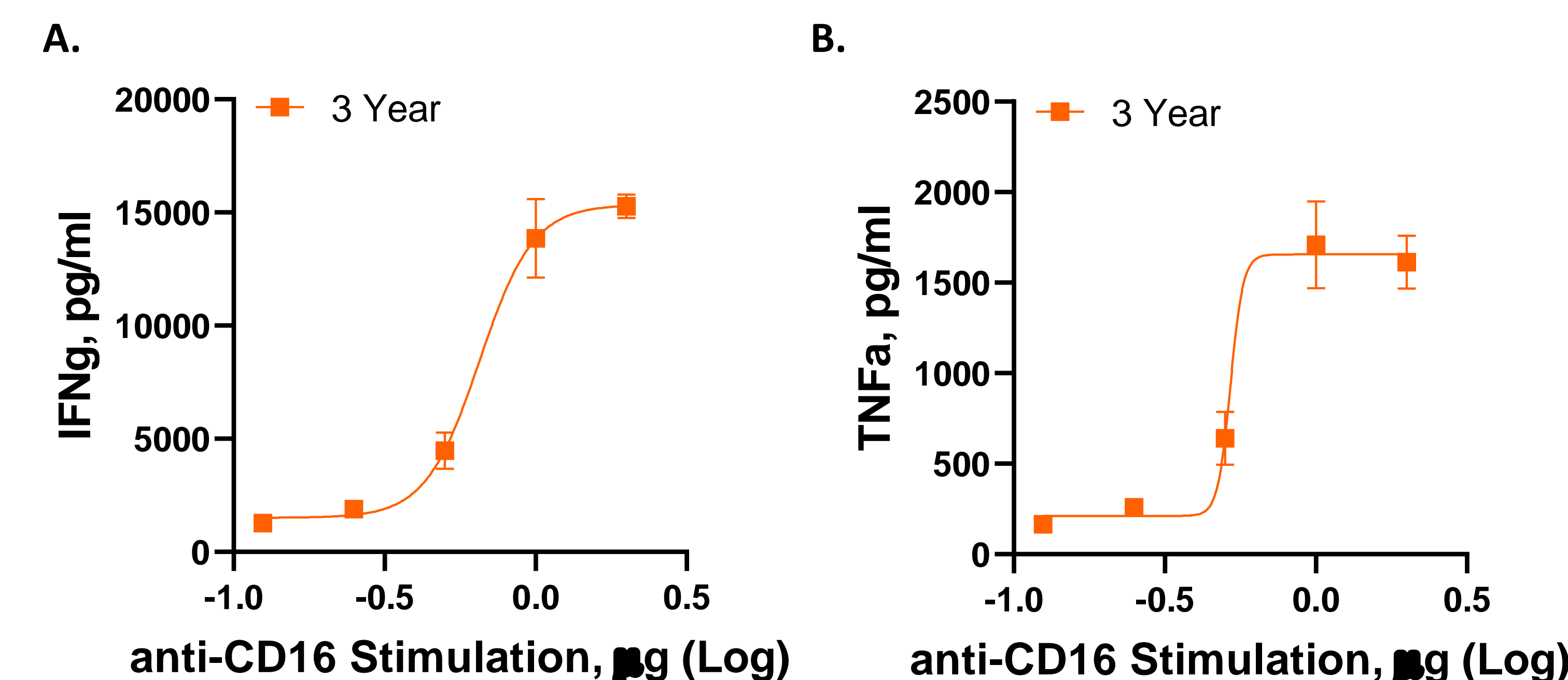
Engineered iPSC-derived iCD34 Intermediate cells can be Stored Long-term and Serve as an Ideal Seedstock for Consistent iNK and iT Cell Production



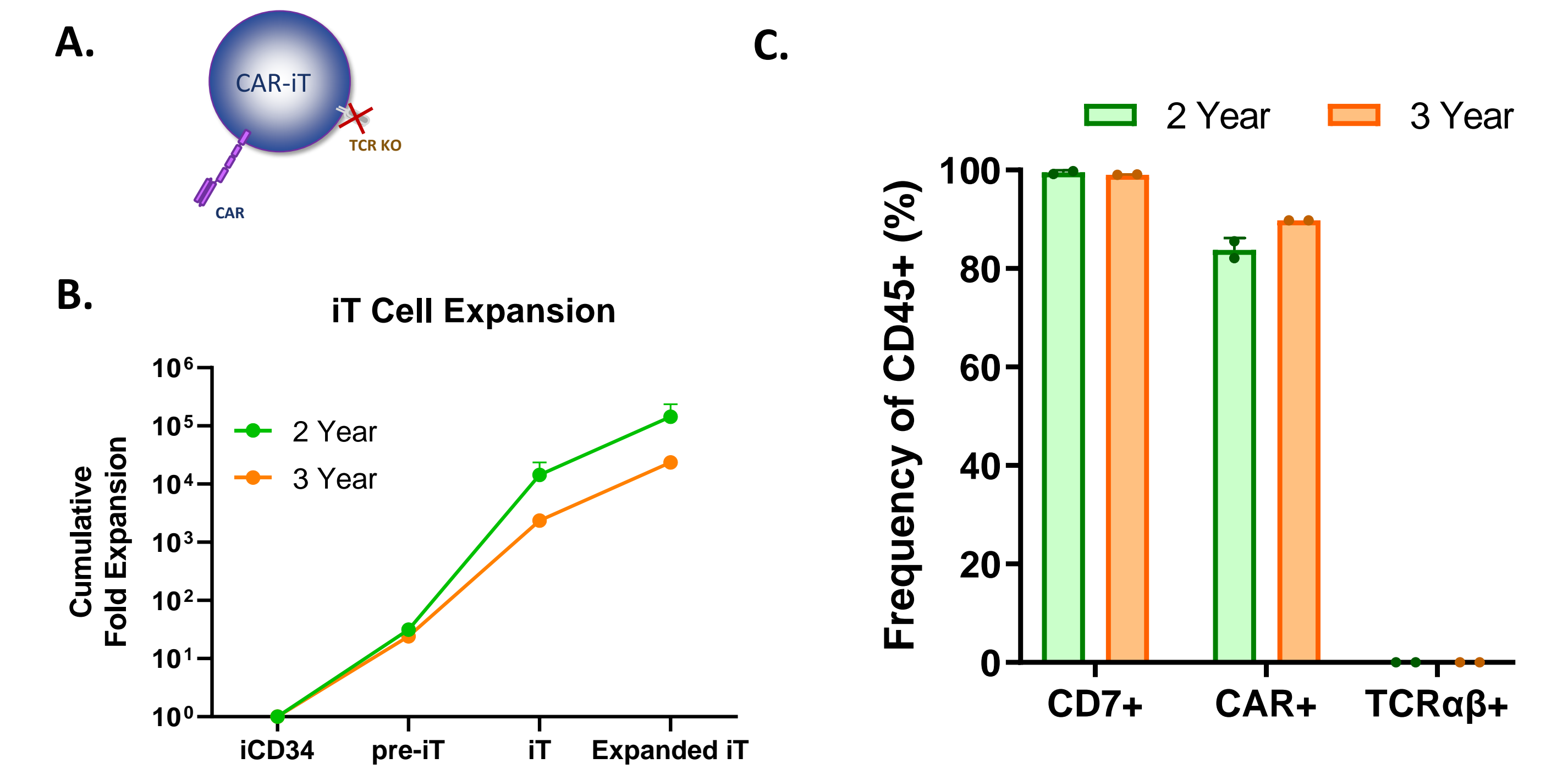
Long-term Cryopreserved iCD34 cells well Support iNK Cell Production



iNK Cells Produced from Cryopreserved iCD34 Cells Support Effective ADCC



Long-term Cryopreserved iCD34 cells well Support CAR-iT Cell Production



iNK Cells Produced from Cryopreserved iCD34 Cells Exhibit Potent Innate Cytotoxicity against Tumor Targets

