

End-to-End Automated Manufacturing of Low-Seed CAR-T Cells

Data presented at the 2024
CAR-TCR Summit Europe

29 February 2024

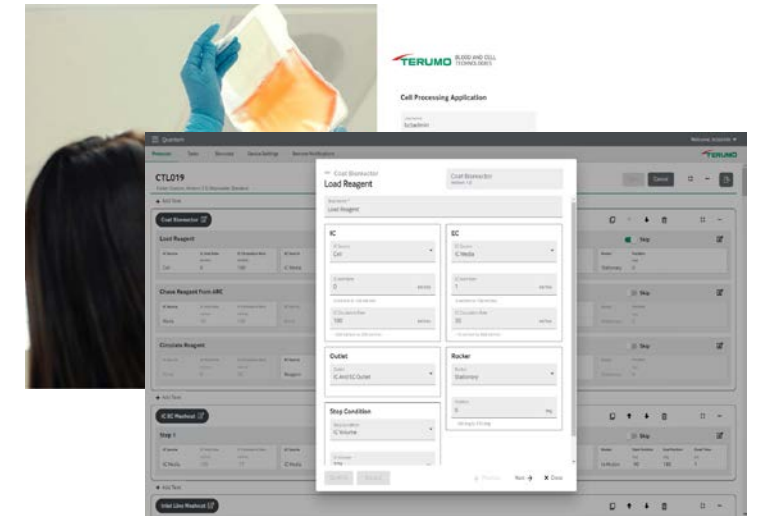
Quantum Flex™ Cell Expansion System



Multiple sizes of hollow-fiber bioreactors enable scalable, perfusion-based cell culture

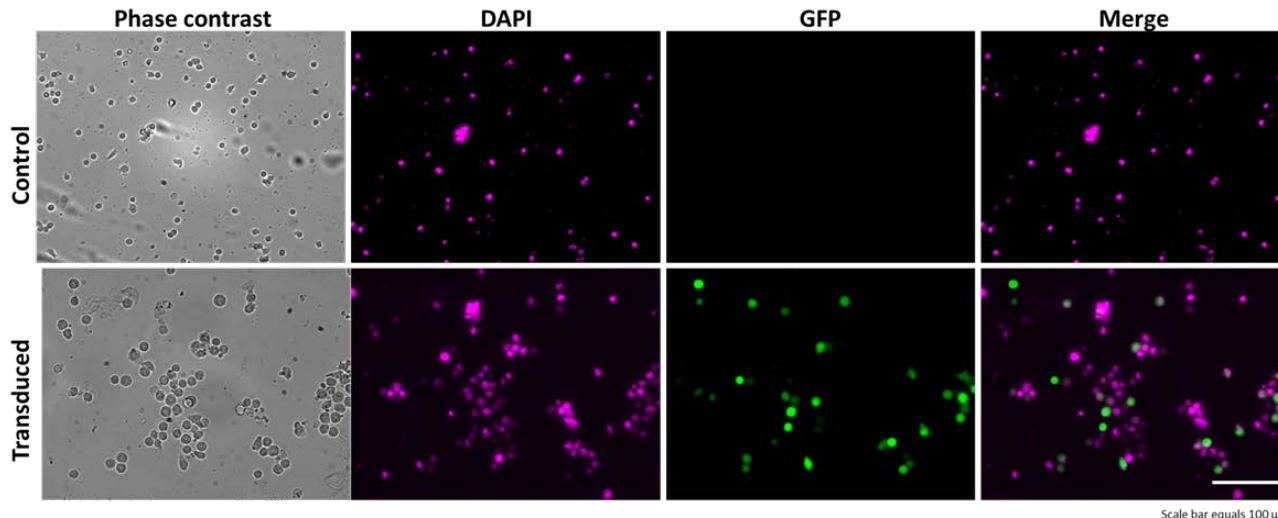
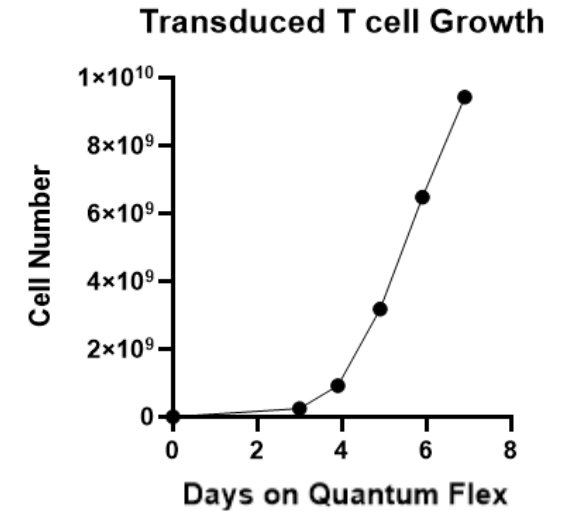
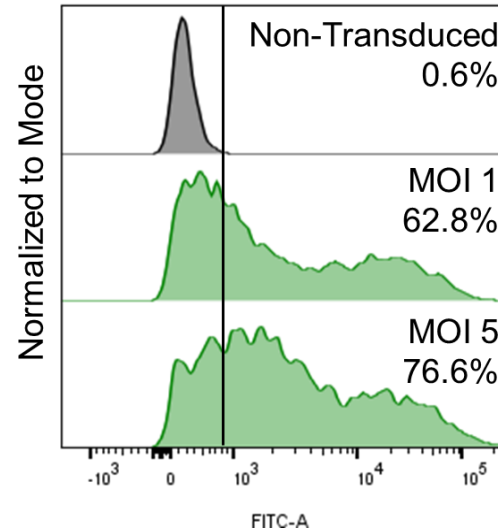
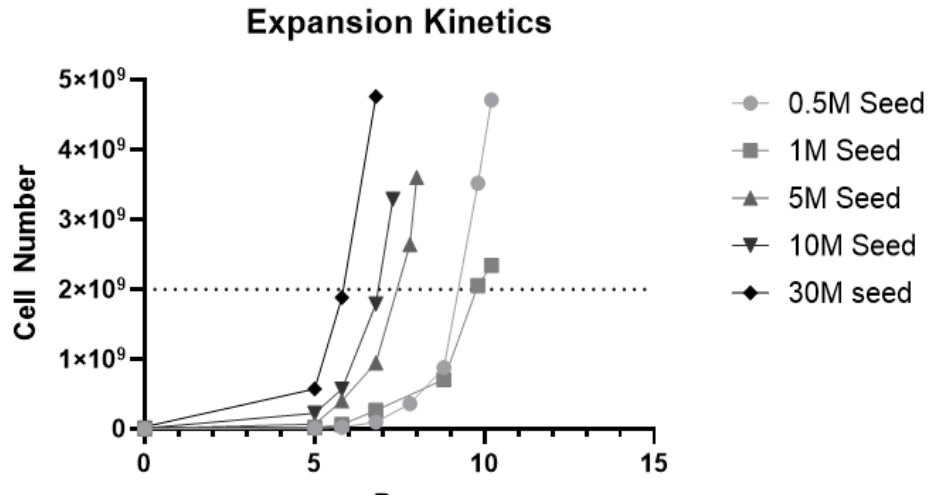


Functionally closed and automated platform expands suspension and adherent cell types



Robust software facilitates fleet and device management and facilitates cGMP/FDA 21 CFR Part 11 compliance

Knowledge Transfer



Successful discovery phase is key to knowledge transfer:

- Maturing processes and technologies
- Assessing feasibility of production to viability and functionality standards
- Addressing variability of starting material
- Piloting talent coordination

Process Development

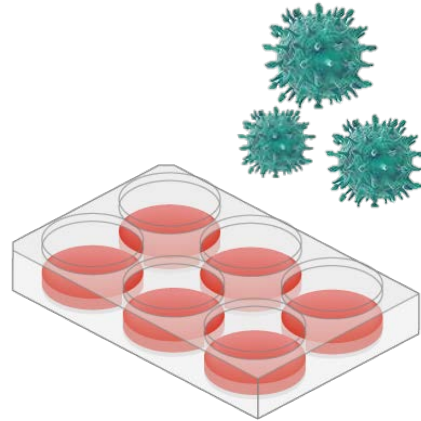
Starting cell material



Cryopreserved adult peripheral blood-derived T-cells

Activated 2 days

Transduction



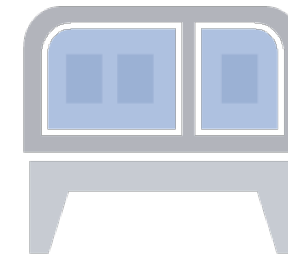
Lentivirus – CD19-CAR

Cell expansion



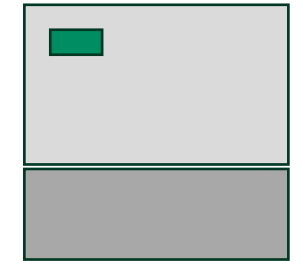
Quantum Flex™

Fill and finish



Finia™
Fill and Finish System

Cryopreservation



Controlled Rate
Freezer

Analysis

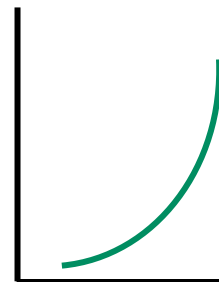
Flow cytometry

- Transduction efficiency
- Phenotyping



Cell expansion features

- Cell numbers
- Viability
- Glucose/lactate
- Cell diameter



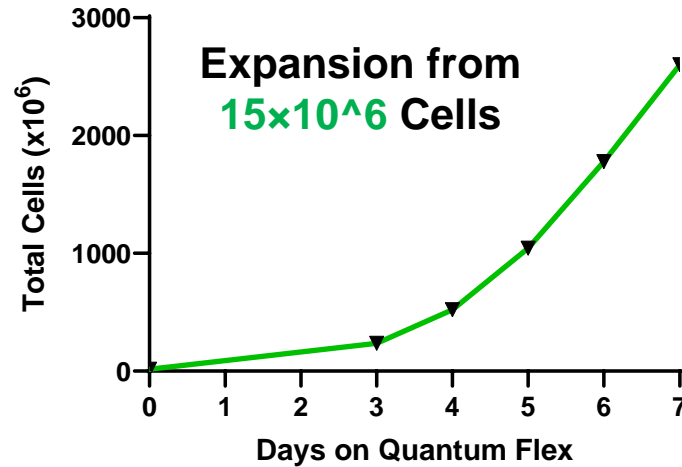
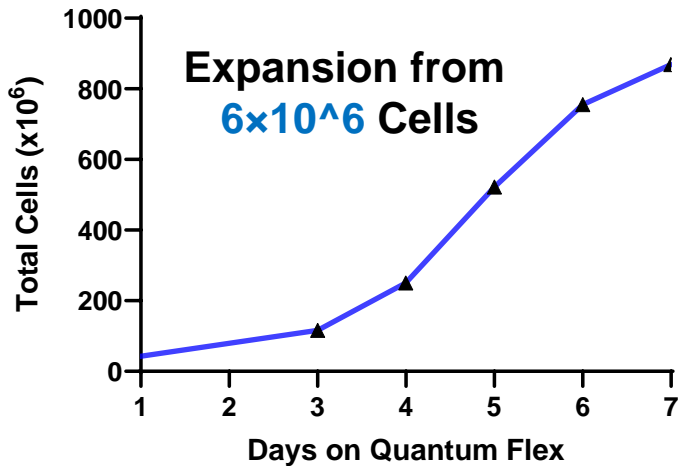
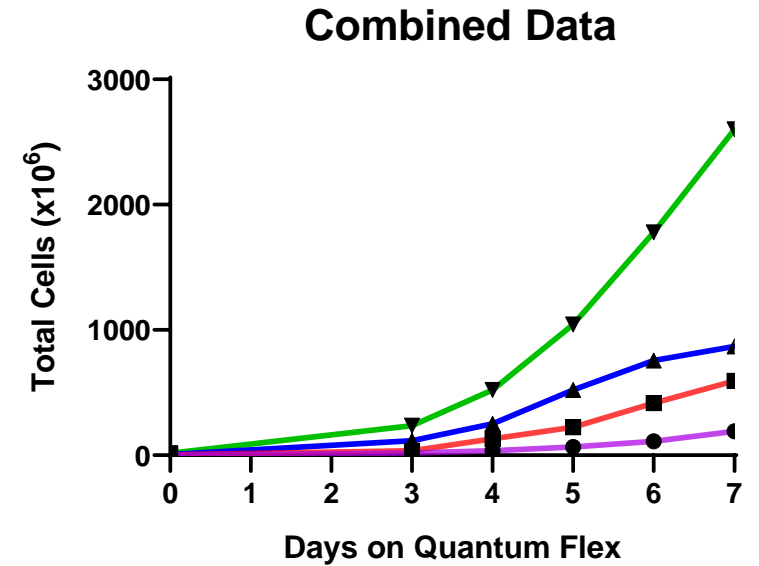
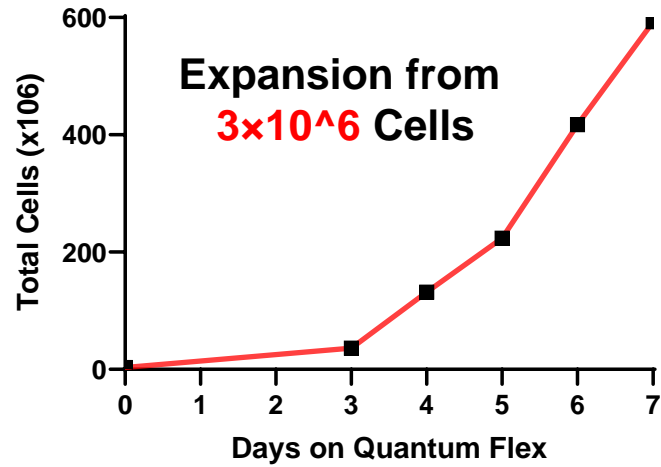
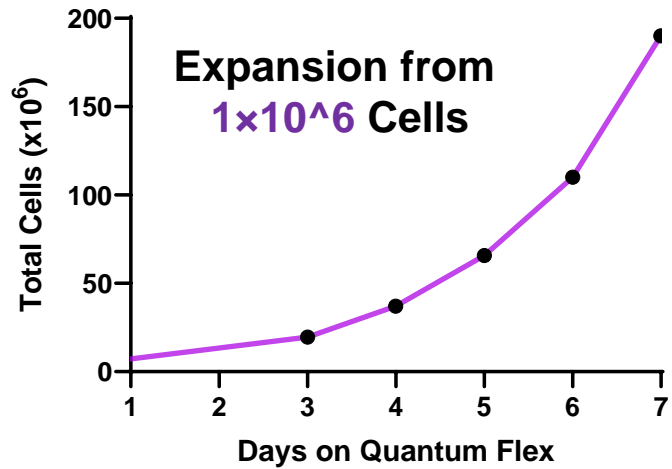
Fill and finish

- Fill volumes (expected vs. delivered)
- Viability
- Recovery

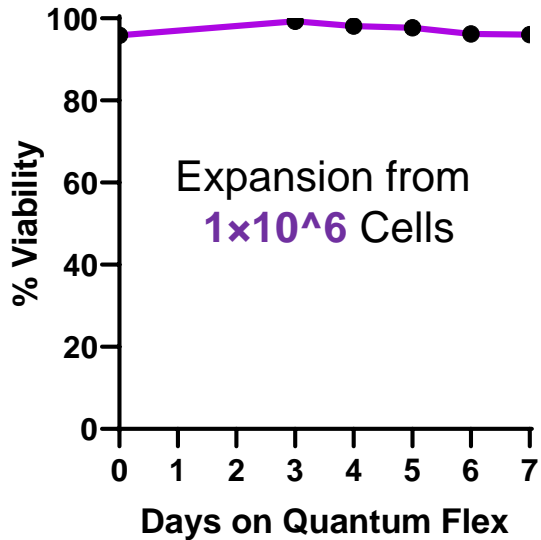
Efficacy

- Potency Assay
- Cell-killing Assay

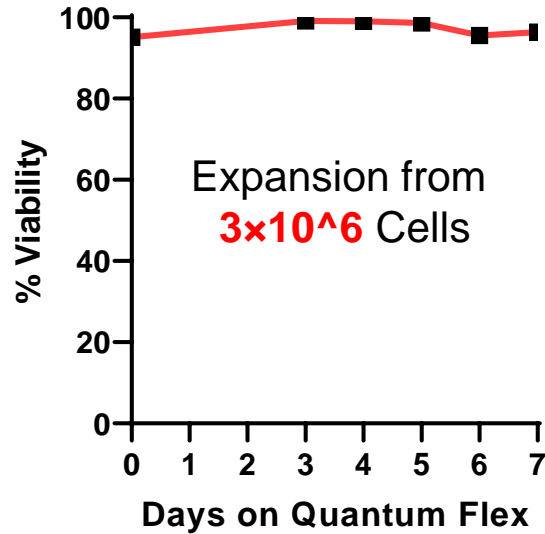
Quantum Flex Cell Expansion of CD19 CAR-T cells



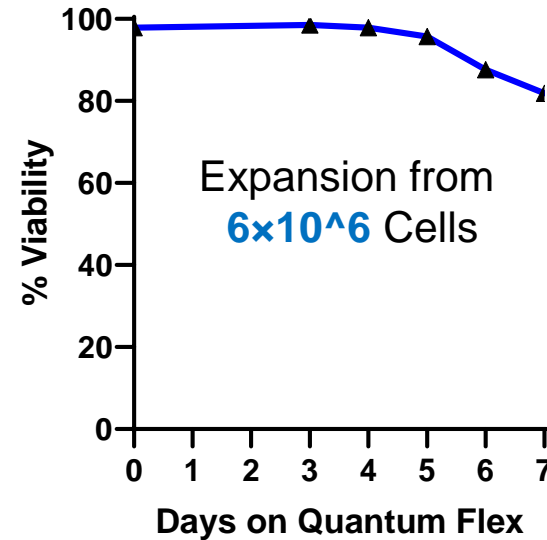
Quantum Flex CAR-T Cell Expansion Shows High Viability



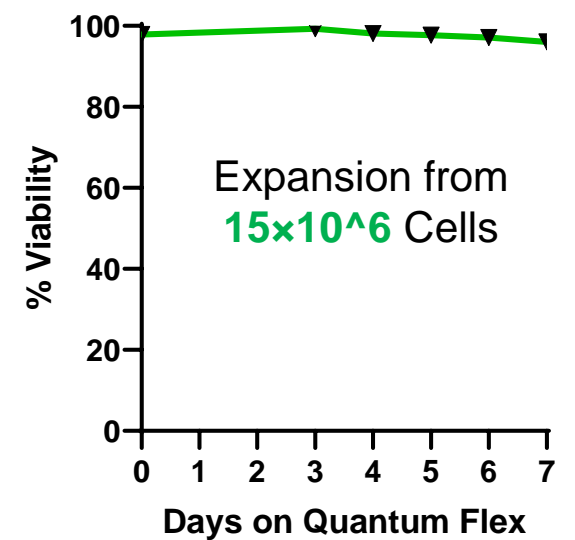
Donor 1



Donor 2



Donor 3



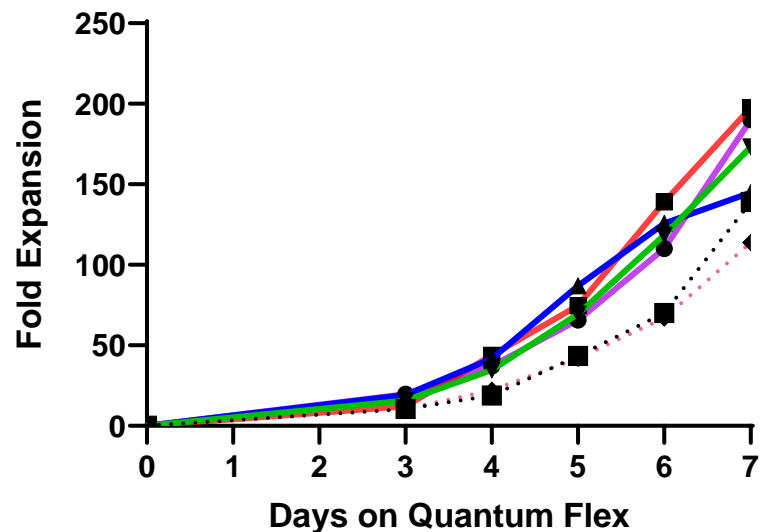
Donor 4

Viability of transduced T cells in the Quantum Flex device did not result in statistically significant differences vs. concomitant control flasks of transduced T cells as assessed by two-way ANOVA with a P value > 0.05 .

Comparable Growth Characteristics

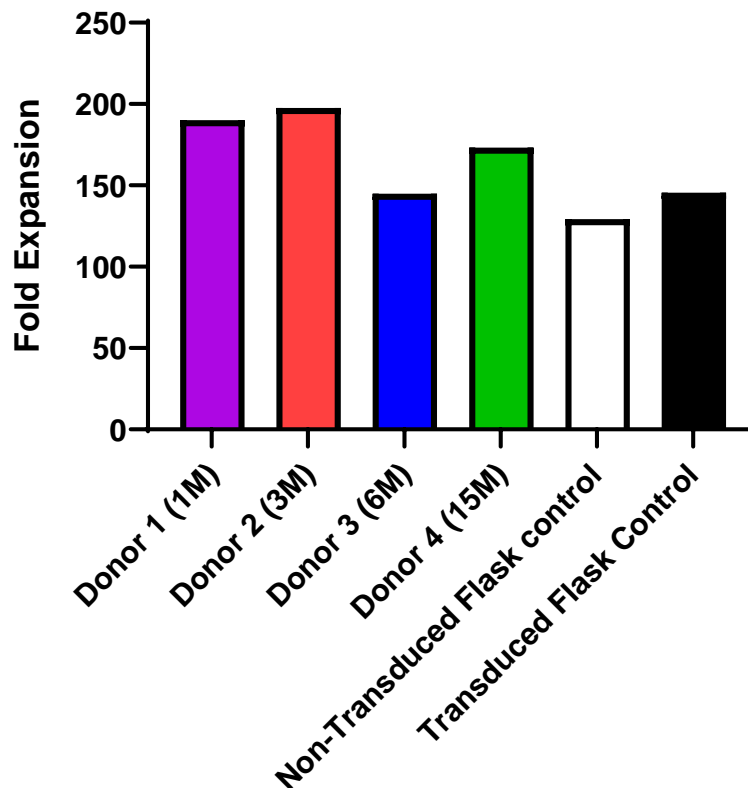


Fold Expansion by Day

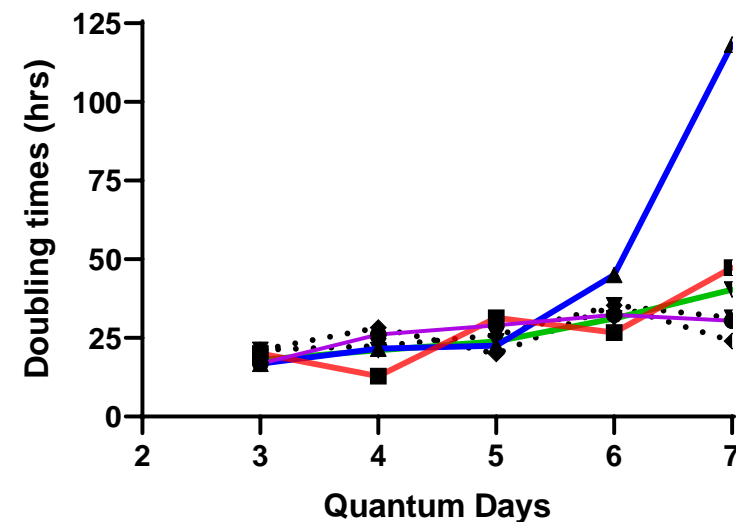


- Donor 1 (1M)
- Donor 2 (3M)
- ▲ Donor 3 (6M)
- ▼ Donor 4 (15M)
- Transduced Flask Control
- ◆ Non-Transduced Flask control

Expansion Totals

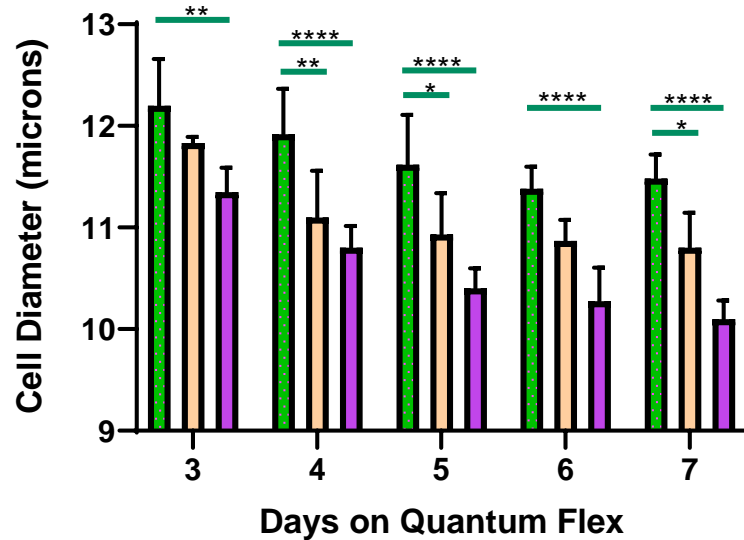


Doubling Times



- Donor 1 (1M)
- Donor 2 (3M)
- ▲ Donor 3 (6M)
- ▼ Donor 4 (15M)
- ◆ Transduced Flask Control
- ▼ Non-Transduced Flask Control

Cell Diameter



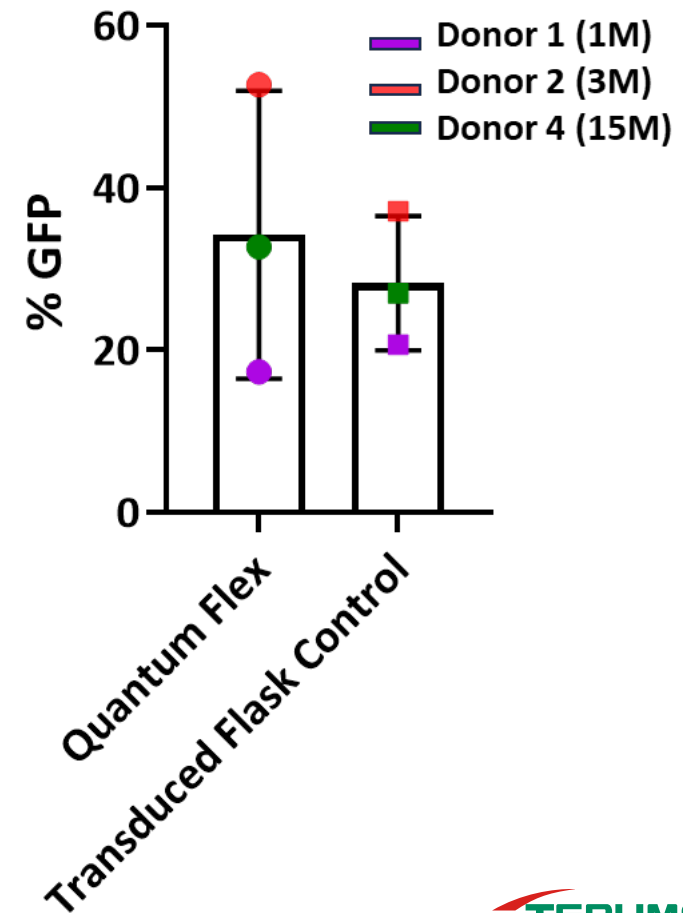
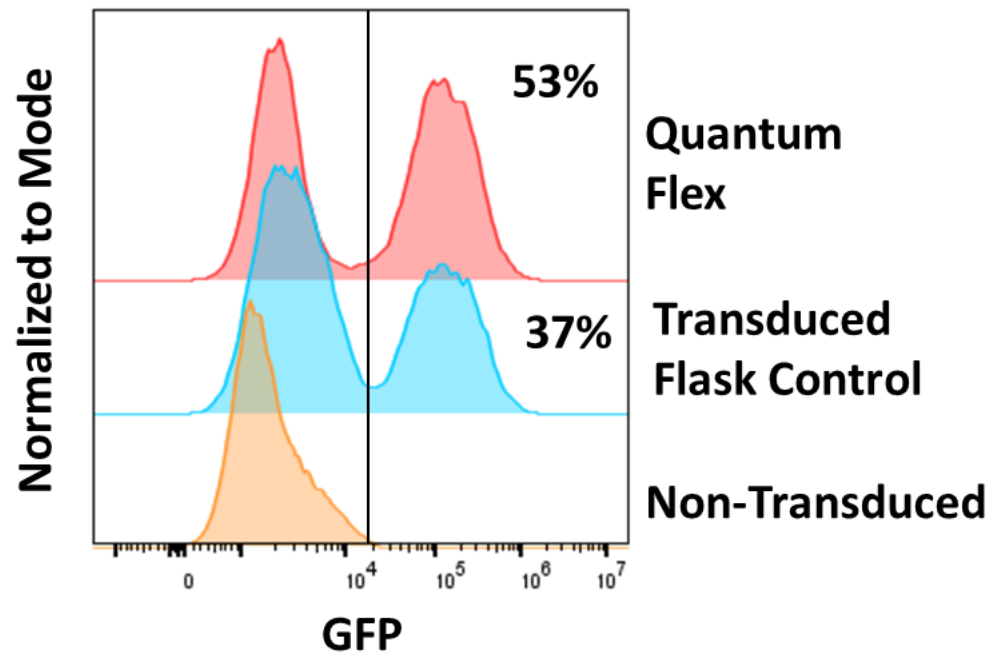
- Quantum Flex
- Transduced Flask Control
- Non-Transduced Flask control

* P value \leq 0.05
** P value \leq 0.01
*** P value \leq 0.001
**** P value \leq 0.0001

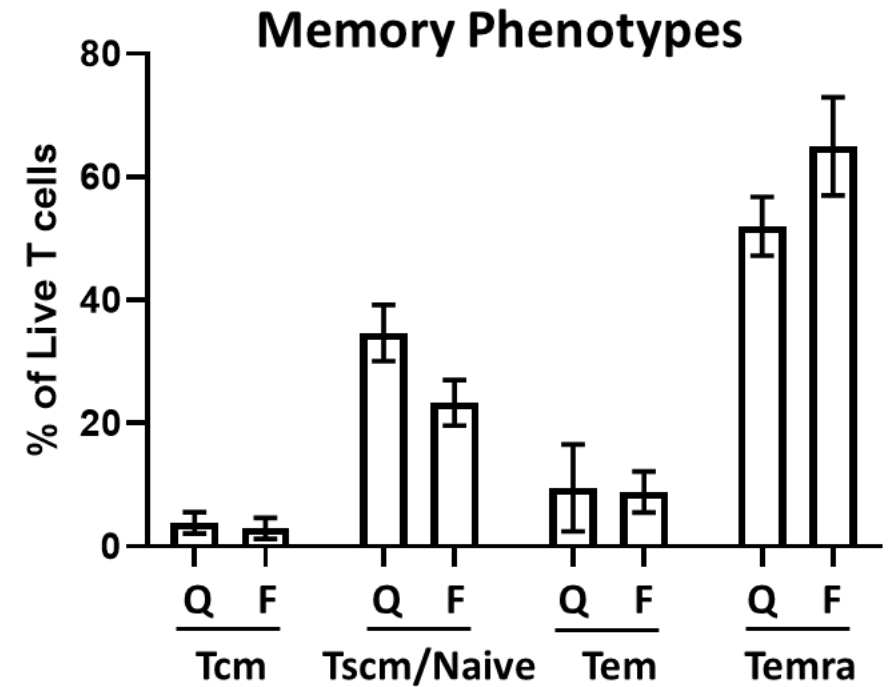
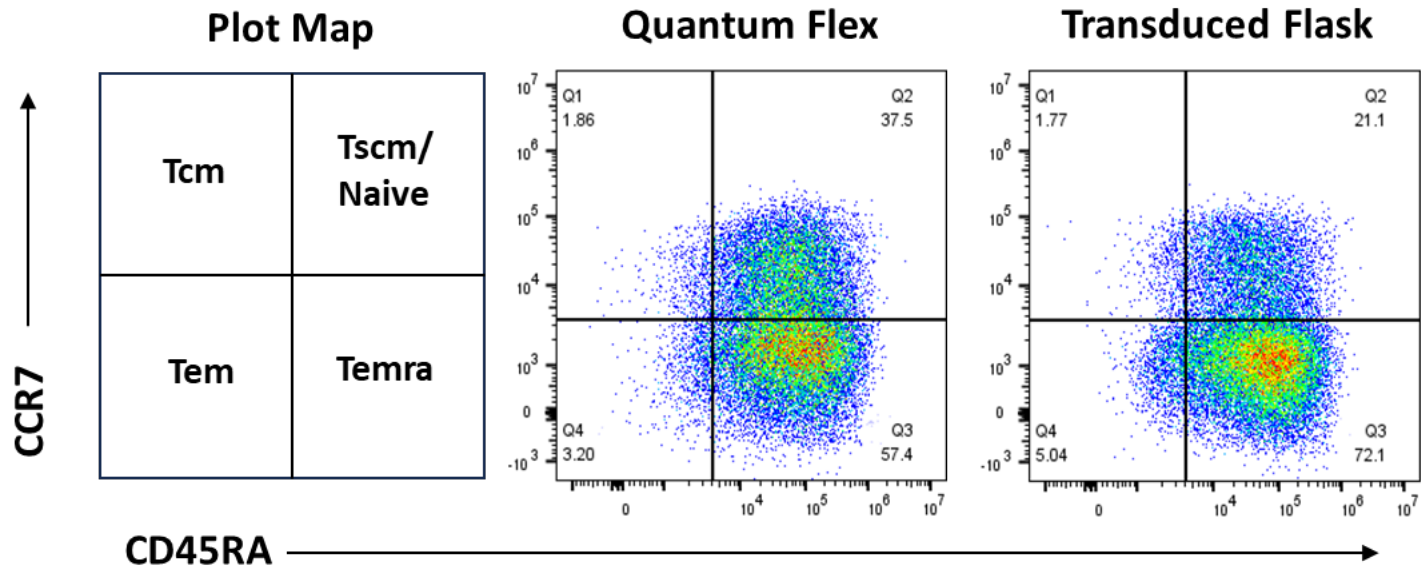
Increased T-cell diameter is associated with cellular activation and expansion

Optimal environment in Quantum Flex may explain the observed high fold expansion of transduced primary T cells

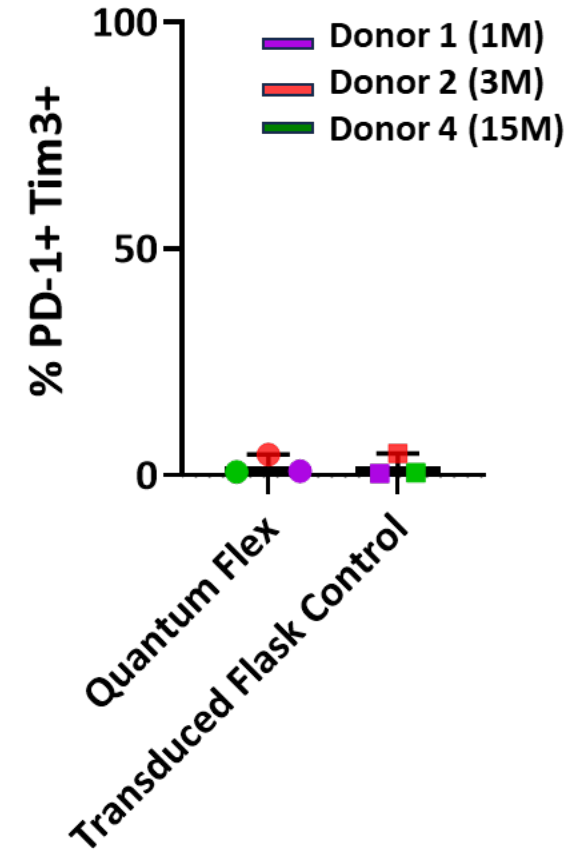
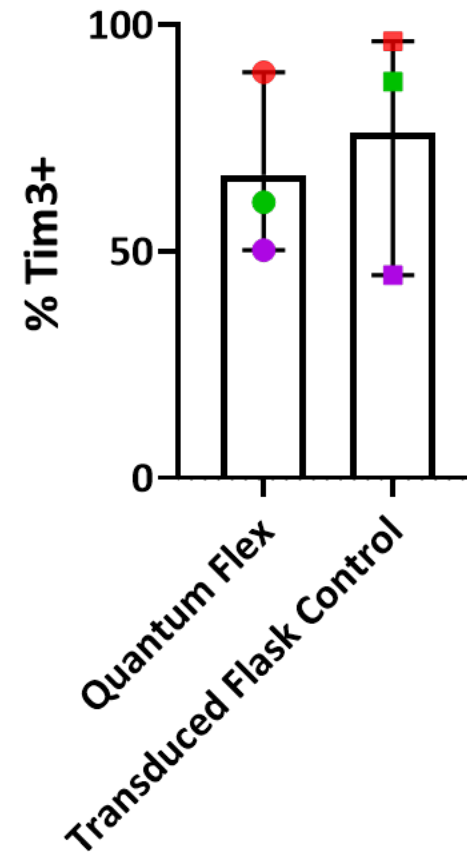
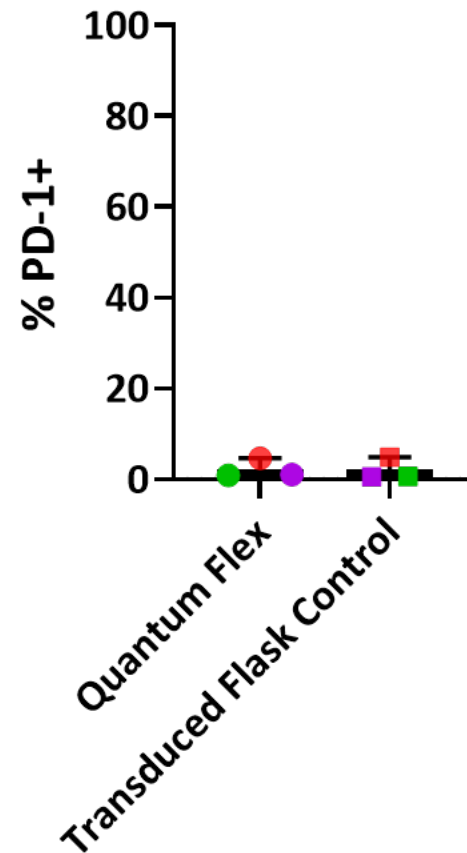
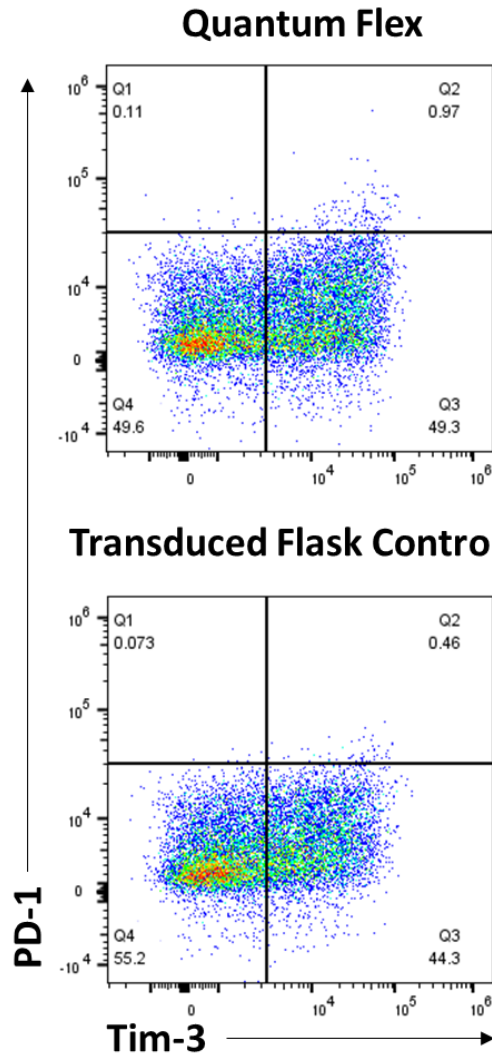
Transduction Efficiency at Harvest



Memory Phenotypes



PD-1 and Tim-3 Expression Are Similar Between Expansion Methods at Harvest



Final Formulation of Expanded CD19 CAR-T Cells



Batch ID 16Feb2024_RI00642B				
FINIA				
Protocol name CS50Training2(2.0)	Date/Time 2/16/2024 11:26:14 AM	Device Serial Number 3F00282	Tubing set 22050	Software version 2.1.1.p01
Quality Control (mL) 11.7 Target 10.0	Product 1 (mL) 18.0 Target 18.0	Product 2 (mL) 18.1 Target 18.0	Product 3 (mL) 17.9 Target 18.0	
Material 1 (mL) 34.4 Target 35.0	Material 2 (mL) 35.0 Target 35.0	Material 3 (mL) 0.0 Target 0.0	Mixing Bag Volume at Procedure Start (mL) 69.4 Target 70.0	
Temperature Set Point: 8.0 °C		Product Flags 10 Volume Tolerance (%) 30 Material 2 Contact Tolerance (min) 10 Material 3 Contact Tolerance (min) 5 Temperature Tolerance (-°C) 5 Temperature Tolerance (+°C)		

- After expansion, CAR-T cells were cryopreserved, but prior to that cells and cryopreservant were formulated by the Finia Fill and Finish System.
- Finia 50 disposable sets have a range of 10 to 28 mL.
- A run report was generated following processing of the cell harvest after expanding from 3 million CAR-T cells.
- Finia formulated the CAR-T cells for cryopreservation with CAR-T cells (Material 1) and Cryostor 10 (Material 2).

Conclusions: Data

- CAR-T cell expansions were performed from four different amounts of starting material (1, 3, 6 and 15 million cells).
- Cell expansion of 150- to 200-fold was achieved, yielding a maximum of 2.6 billion cells in this study.
- Viabilities remained high throughout expansion, with > 95% for 3 of the 4 donors, > 80% for all donors.
- With this range of starting numbers of CAR-T cells, the platform is relevant to adult, pediatric, and compassionate CAR-T dosing.
- This study was a detailed investigation into the expansion of CAR-T cells on Quantum Flex and the final formulation on Finia as part of the strategic collaboration between BioCentriq and Terumo Blood and Cell Technologies.

Data on file as reference at Biocentriq and Terumo Blood and Cell Technologies.

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Thank You

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