# Simple magnetic cell separation enabled by an automated, closed system for both autologous and allogenic cell therapy development

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## Introduction

Adoptive cell therapy has proven clinical efficacy in many cancer types and the success has driven more development of new drugs. However, on the manufacturing side, current process using conventional tools is complicated and results in suboptimal purity and yield sometimes. All those shortcomings may contribute to the high cost of the cell products and limit the patients access to drugs. Cell therapy developers in both industry and academic settings are trying to improve their manufacturing process aiming to increase efficiency and lower cost. Cell selection done with magnetic beads antibody conjugate is an important step in cell manufacturing: it is either the first step to isolate T cells for gene modification or the last step to deplete subtype of T cells in allogenic transplantation, so a fast efficient magnetic cell separation system has been desired. We have developed an automated closed system (MARS® BAR) based on Applied Cells proprietary column-free matrix-free in-flow magnetic cell separation technology. The system can deal with diverse cell sources without requiring cell washing before or after labeling, thus it makes the cell selection workflow very simple. The MARS® BAR system has no capacity limit and is easy to scale-down or scale-up, which makes it suitable for both autologous and allogenic cell therapy manufacture.

## Method

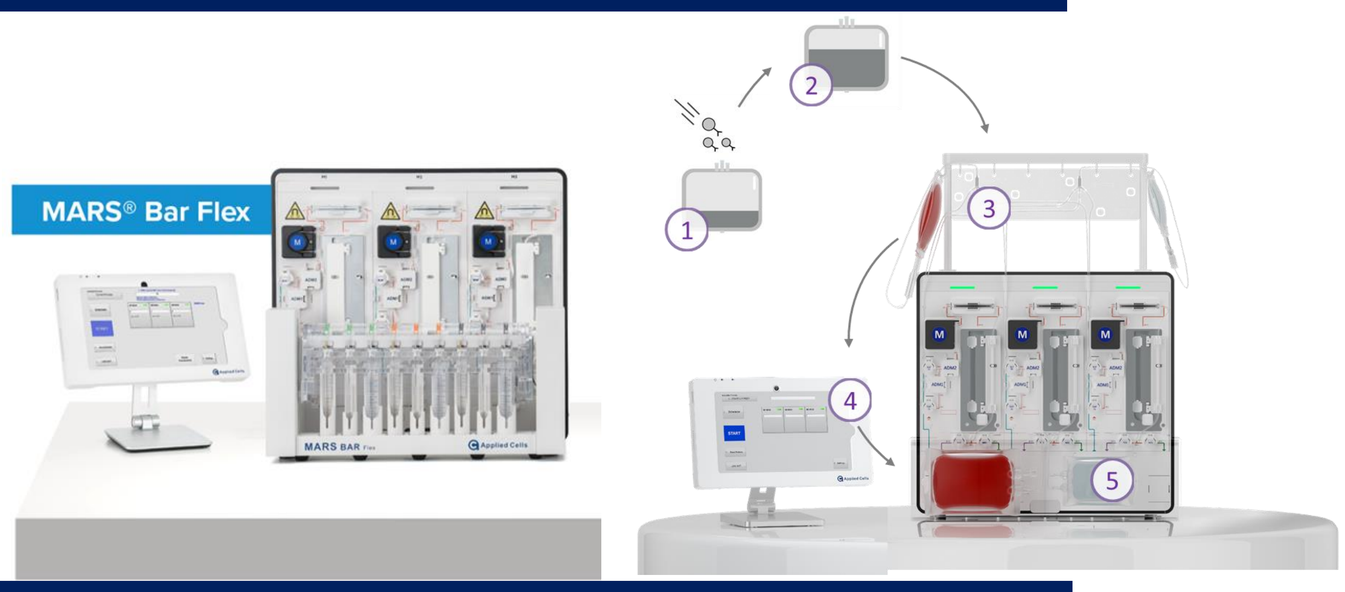
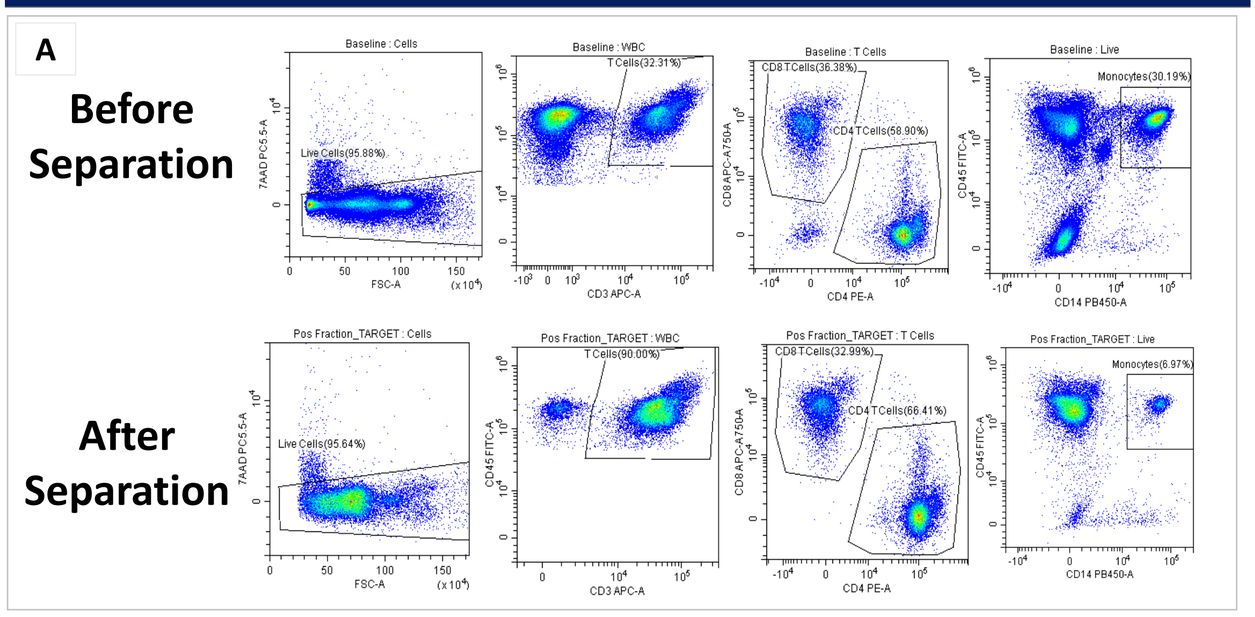
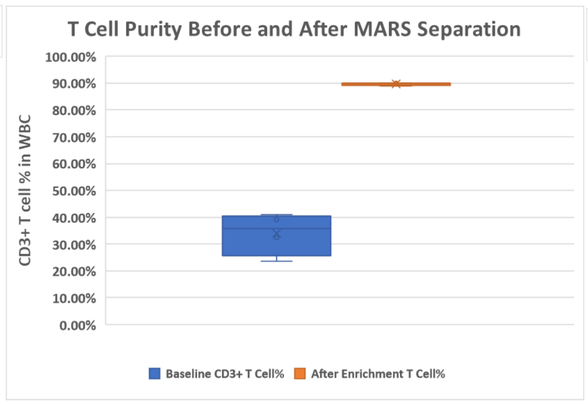


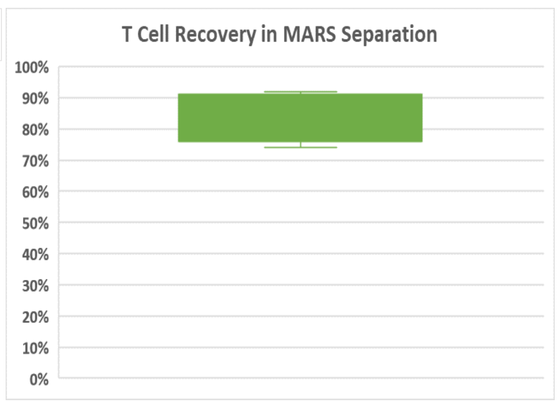

**Figure 1. Schematic image of MARS® BAR cell separation platform.** On the left is the MARS Bar Flex system (tube-in-tube-out), which is used for small scale process development. On the right is the MARS Bar with single-use closed tubing set (bag-in-bag-out). 1-5 are operation steps for MARS Bar cell separation: 1, magnetically label target cells – add CD4 and CD8 nanomagnetic beads to sample bag containing leukapheresis product; 2, incubate at 4°C on a rocker; 3, connect sample bag to the tubing set with thermo sealer and install tubing set; 4, select program and run; 5, collect isolated T cells in the bag.

## Results

### 1. Automated T Cell Separation



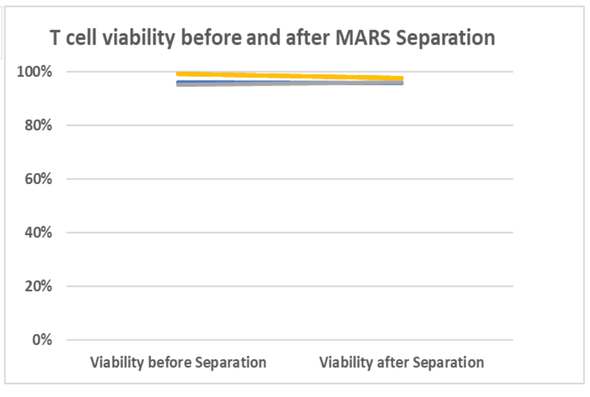




**Figure 2. MARS Automated T cell selection results from frozen and fresh leukopak of healthy donors. Total cell count of four samples are 6 million, 32 million, 1 billion and 2.7 billion.**
A, flow cytometer analysis of cell composition before and after separation. B, C and D, T cell purity, Recovery and viability before and after separation.

### 2. T Cell Expansion and Phenotypic Analysis

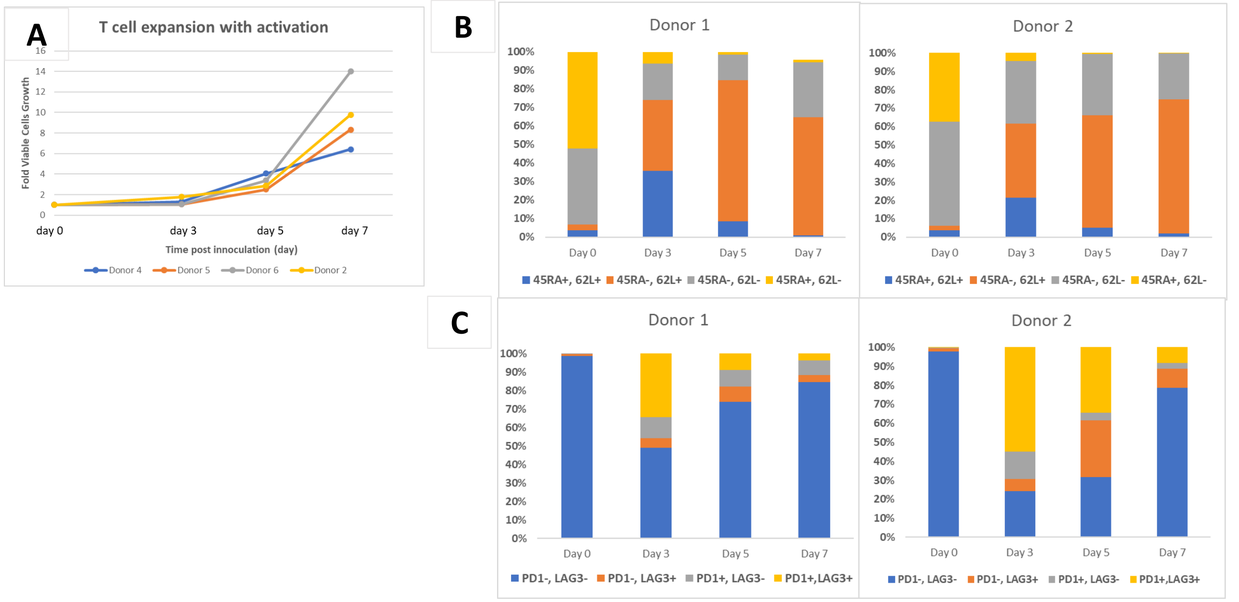



**Figure 3. Isolated T cells culture expansion and phenotypic analysis over 7 days of expansion.** A. T cells isolated on MARS have 6-14 folds expansion with activation using ImmunoCult™ Human CD3/CD28 T Cell Activator. B, T cell subtype analysis. C, T cell exhaustion markers. B and C analysis show central memory T cells (CD62L+CD45RA-) dominant over 7 days of culture.

## Conclusions

- **Scalability** -- Here we show the automated T cell separation on MARS Bar platform at small (million) and large (billion) scale using the same protocol and getting consistent results
- **Economical solution –** MARS Bar offers the very simplified sample preparation and saves multiple washing steps, thus provides a time-saving and cost-saving solution
- **Gentle process –** MARS column-free magnetic cell separation maintains cell viability and functionality

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