Novel Multiphysics Cell Separation Platforms for Cell Therapy Development

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PRESENTED AT ISCT 2022

Applied Cells

INTRODUCTION

In the past twenty years, cell therapy has made great success in treating patients and enormous efforts have been devoted to developing new drugs as well as improving the efficiency of manufacturing processes. New technological solutions with flexibility and scalability are desired to support the promise of cell-based therapy. MARS® Cell Separation Platforms incorporate innovations in multiple cell separation technologies to provide solutions for cell therapy manufacturing challenges. MARS® platform offers a column-free in-flow magnetic cell separation technology, which allows a specific selection of cells based on their surface markers. The separation process is done in a closed fluidic path in a fully automated fashion and has no capacity limit. The MARS® active acoustic cell separation uses an acoustic standing wave established in a microfluidic chip to move cells in or out of their fluidic stream to achieve cell washing and concentration automatically. Here we present a few use cases of MARS® technologies to demonstrate the unique capability in cell separation.

METHODS

Target Populations in 1mL Leukopak Sample					
Cell Type	Live WBC	T Cells	CD8+ Cells	CD4+ Cells	B Cells
Count	88E6	54E6	16E6	34E6	12E6
% Live WBC	100%	61%	18%	39%	14%

Table 1. Cells from fresh leukopak samples were characterized using a flow cytometer with multi-color antibody staining and viability dye 7AAD.

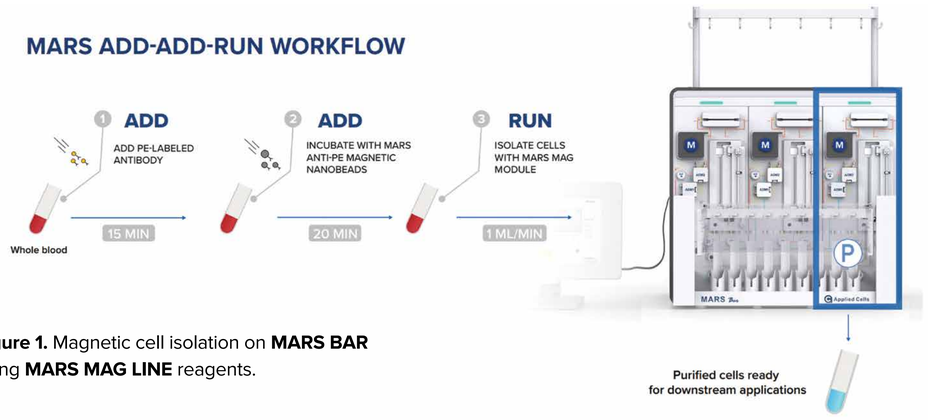

Figure 1. Magnetic cell isolation on **MARS BAR** using **MARS MAG LINE** reagents.

Figure 2. MARS SP instrument was used to purify PBMCs from fresh or frozen leukopak with the Acoustic Cell Processing Chips built-in without centrifugation steps.

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RESULTS

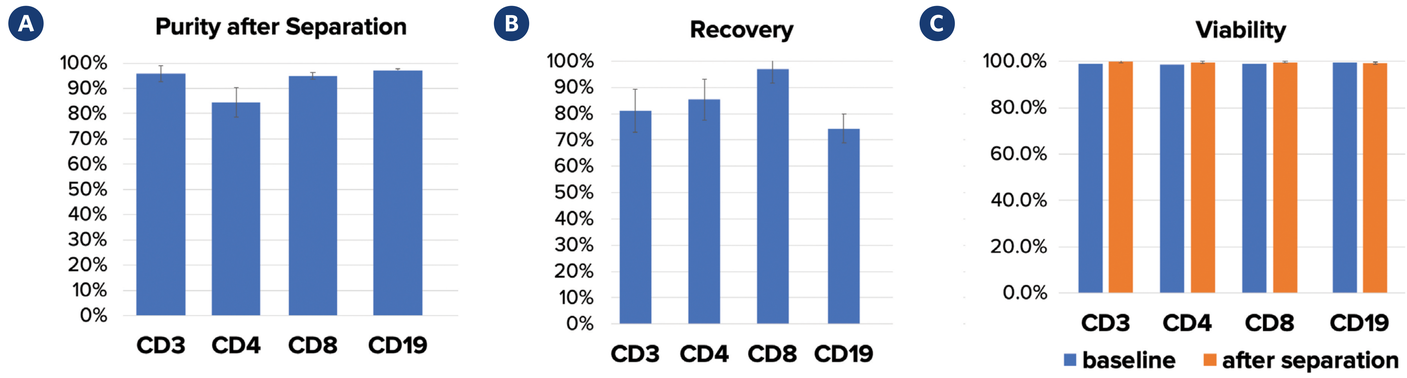

Figure 3. MARS BAR enables automatic magnetic cell isolation of immune cells from leukopak with high purity, high recovery, and high viability at 3mL/min flow rate (~200e6 per min) **A**, cell purity was accessed by flow cytometer analysis. Note: CD4 was also expressed on monocyte so there was some contamination from monocytes. **B**, cell recovery was calculated by cell count after separation divided by the baseline of x100%. **C**, cell viability before and after separation was accessed by 7AAD staining of cells. (*n range from 3 to 7)*

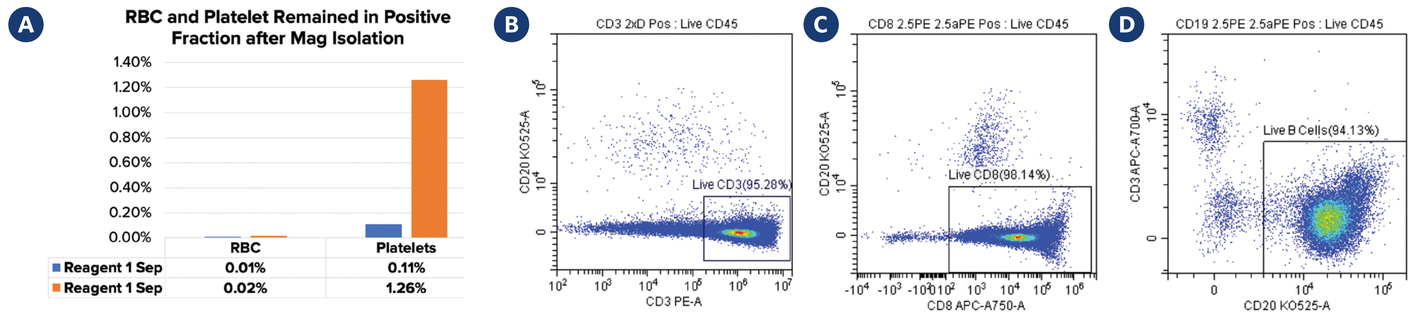

Figure 4. MARS BAR positive selection of cells minimizing contamination of other immune cells as well as red blood cells and platelet. A, MARS positive magnetic separation isolates cells directly from leukopak sample with minimum dilution and removes red blood cells and platelet without RBC lysis and centrifugation. **B, C, and D**, representative flow cytometer plot of isolated CD3+ cells, CD8+ cells and CD19+ cells.

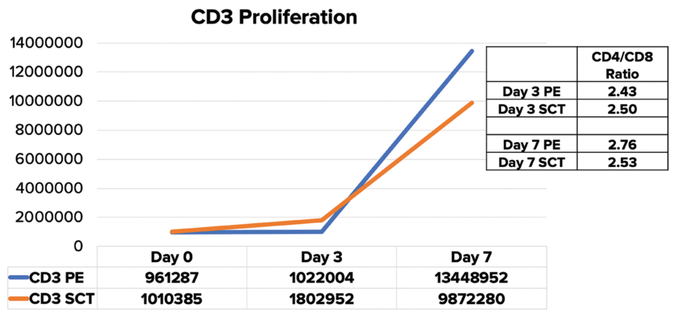

Figure 5. MARS BAR isolated T cells showed robust expansion after activation.

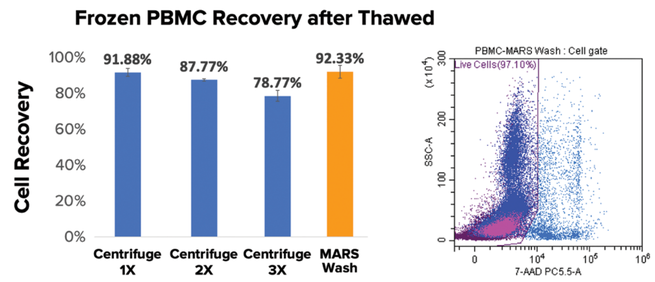

Figure 6. MARS acoustic cell washing on SP system was able to isolate PBMC from DMSO containing media and recover viable cells.

SUMMARY

- MARS® BAR magnetic cell separation system allows isolation of T cells and B cells directly from leukopak in a closed fluidic path
- MARS® BAR Isolated cells have shown high purity, high recovery, and high viability
- T cells can proliferate upon activation
- MARS® SP acoustic washing isolates PBMCs from DMSO containing media without involving centrifugation steps and shows better recovery than the centrifuge process