

Closed and Automated Cell Processing Using Rotea™ to Advance Cell Therapy

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ABSTRACT

The manufacturing cost and complexity has been one of the biggest obstacles for delivering cell therapy products. Here we present Rotea™, a compact closed automation system with counterflow centrifuge technology, which enables gentle cell separation, wash, and concentration with controllable input and output volumes. The 10ml chamber on the single use kit can sustain billions of cells as a fluidized bed and can be discharged multiple times if needed. The kit can be easily connected to other closed systems for upstream and downstream applications, for example Finesse bioreactor system, making Rotea a flexible modular instrument to fit in different workflows.

Using human primary T cells as a model, we have demonstrated that across different input and output settings, Rotea contributes superior processing time, recovery, and viability for cell wash, concentration, and buffer exchange as compared to manual centrifugation. More importantly, Rotea is capable of facilitating lymphocyte separation from leukopheresis products, which could shorten manufacturing time and cost of cell therapy products.

INTRODUCTION

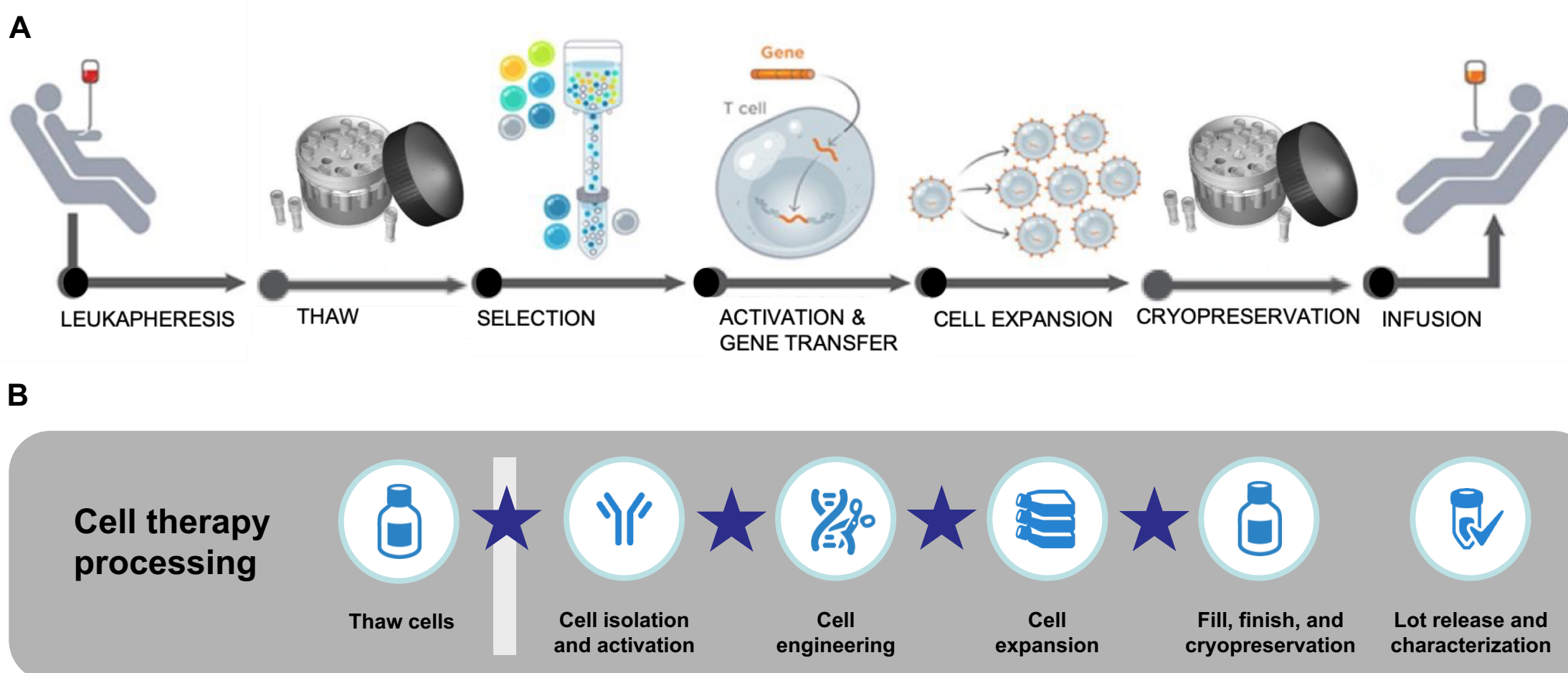


Figure 1. Current cell therapy workflow. (A) Current processes rely heavily on cell isolation, wash, and concentrate. Automated processing in each step indicated in (B) could increase the efficiency and lower the cost of cell therapy manufacturing.

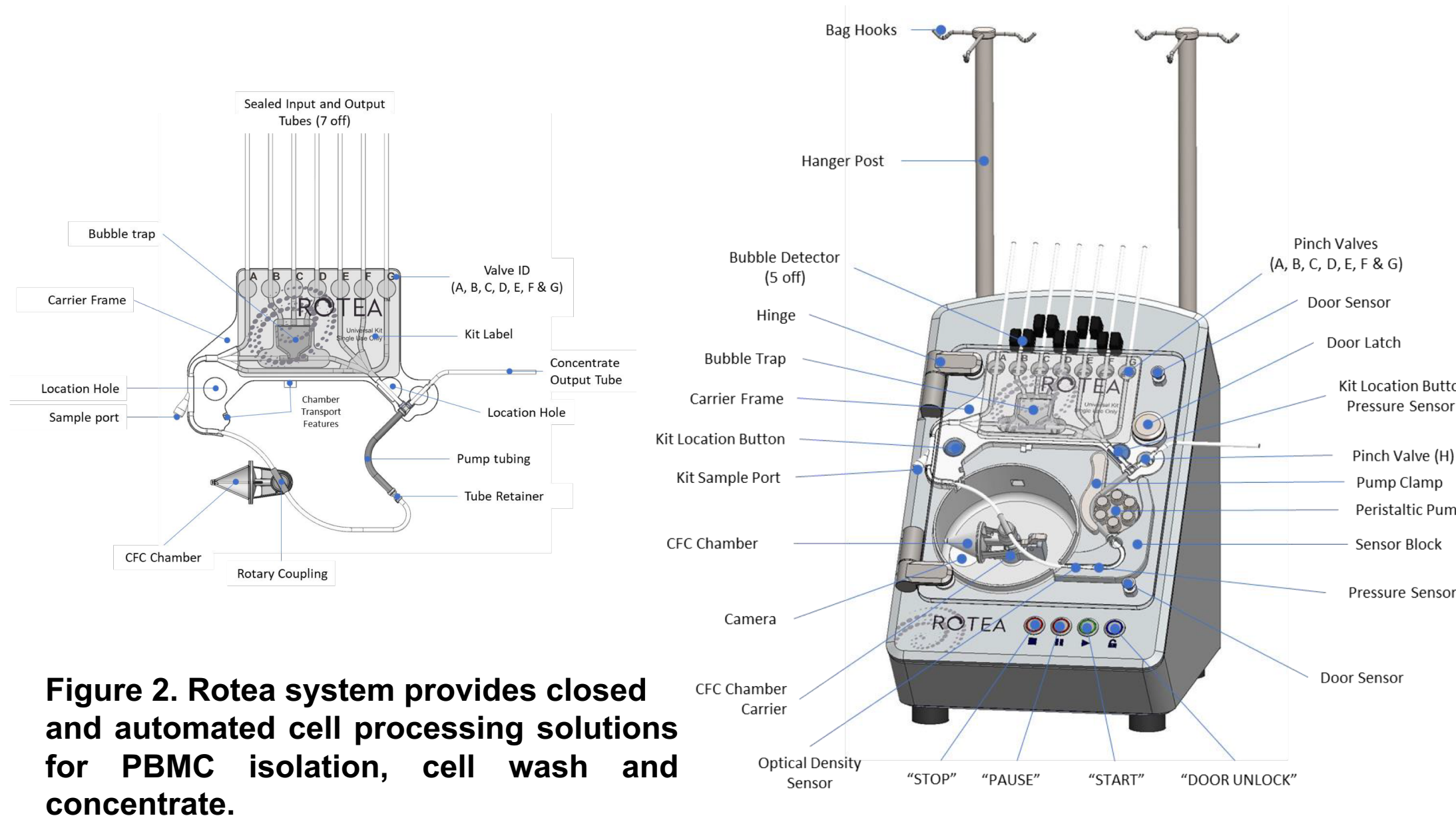


Figure 2. Rotea system provides closed and automated cell processing solutions for PBMC isolation, cell wash and concentrate.

- **Scalable throughput**- continuous processing of 0.1 to 20L
- **Small minimum output volume**- less than 5mL
- **Flexible**- programmable, multiple processing modes including cell separation, concentration and washing
- **Universal kit** (consumable) for different cell types and applications
- **Compact and portable**
- **User friendly**- easy to load, friendly user interface

DEVELOPMENT STRATEGY AND RESULTS

PBMC Isolation Using Rotea

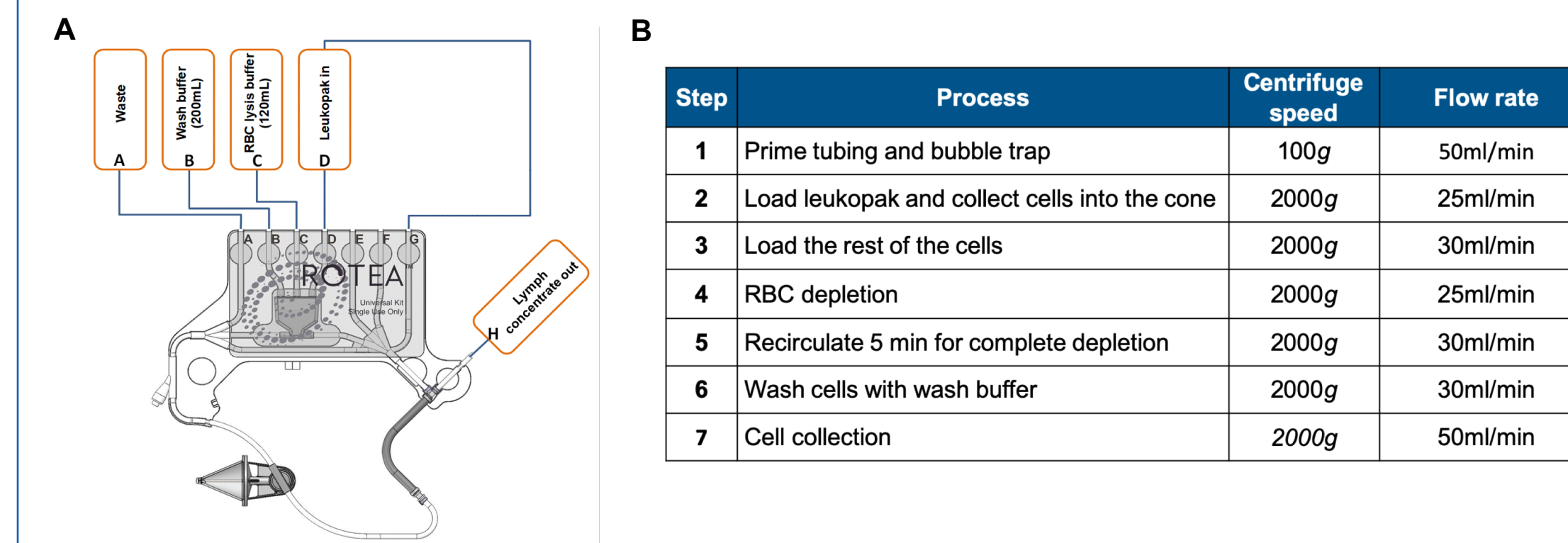


Figure 3. Consumable setup and protocol for PBMC isolation using Rotea. (A) Schematic diagram of Rotea single-use kit connecting with bags for input, output, and buffers. (B) Automated steps for Rotea PBMC isolation.

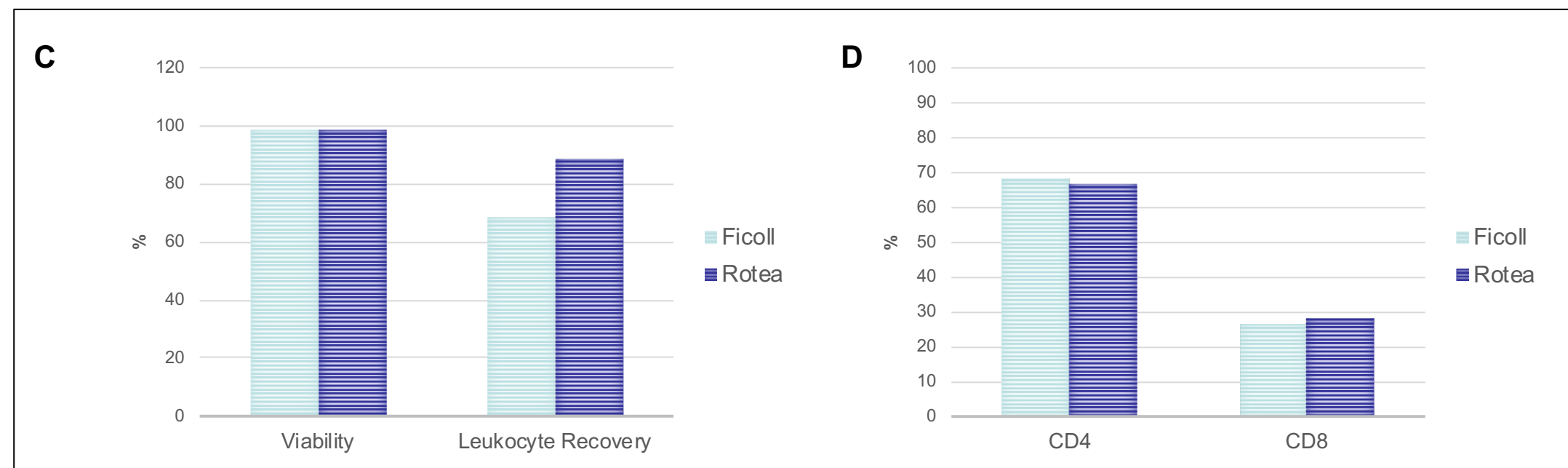
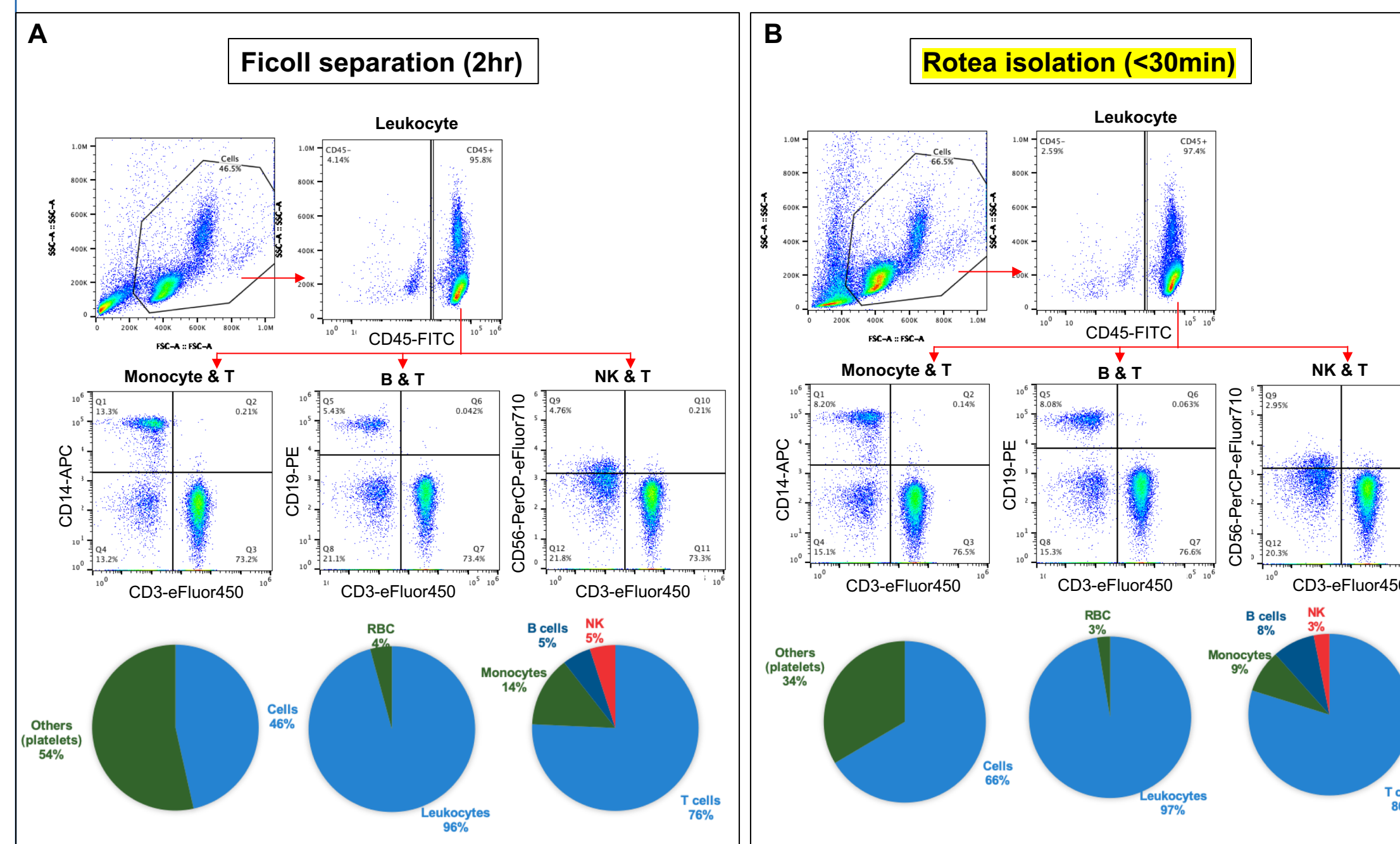


Figure 4. Rotea provides higher quality and efficiency of PBMC isolation as compared to Ficoll separation. (A and B) Rotea completes PBMC isolation in 30 minutes with thorough platelet and RBC depletion. (C and D) The viability, recovery and T cell composition from Rotea PBMC isolation are equal or better than Ficoll separation.

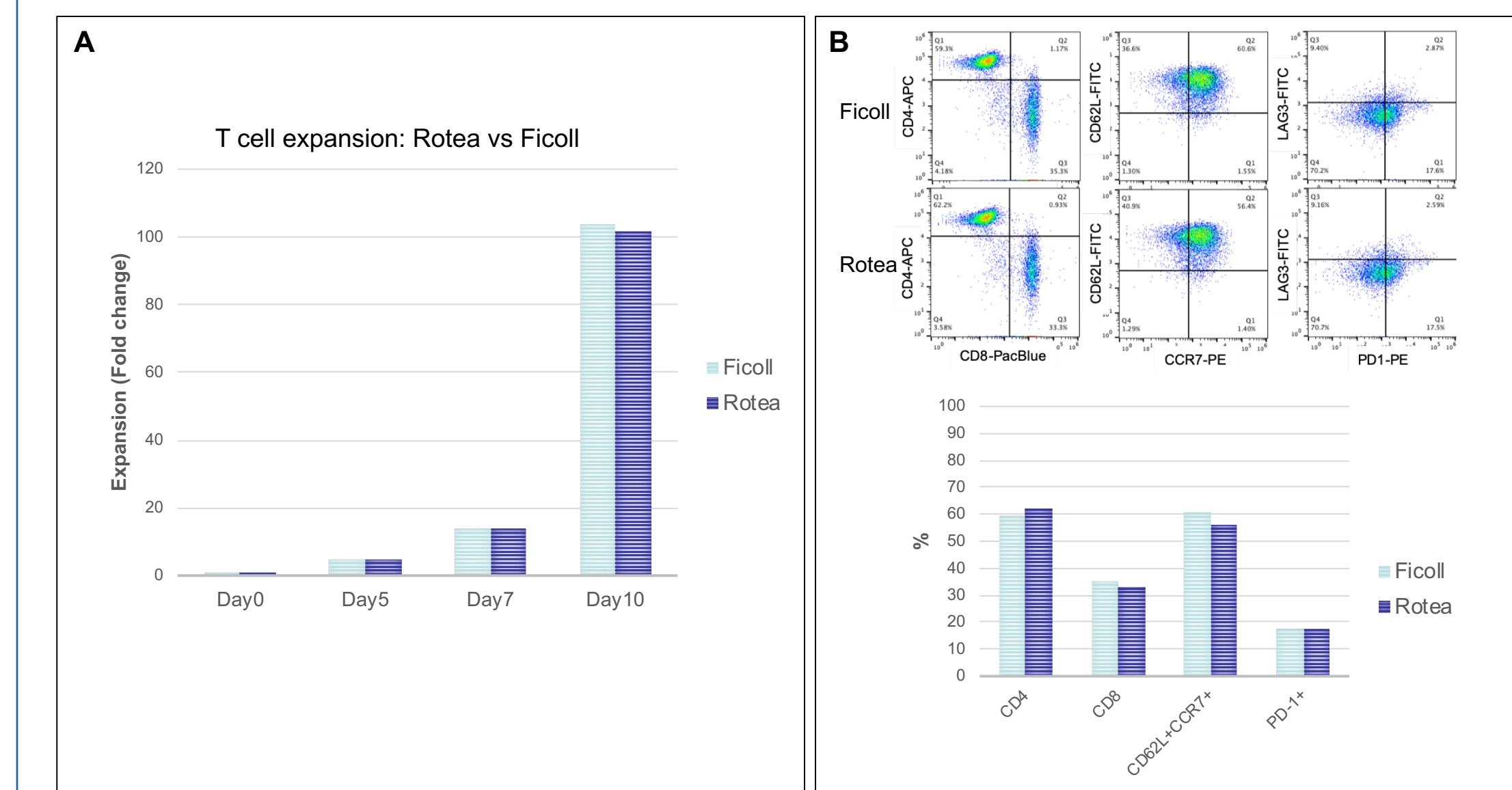


Figure 5. T cells processed from Rotea exhibit similar quality as compare to Ficoll control throughout expansion. (A) The expansion rate of T cells after Rotea and Ficoll processing. (B) T cell composition, differentiation and exhaustion status are similar between Rotea and Ficoll samples after expansion.

T Cell Wash and Concentrate Using Rotea

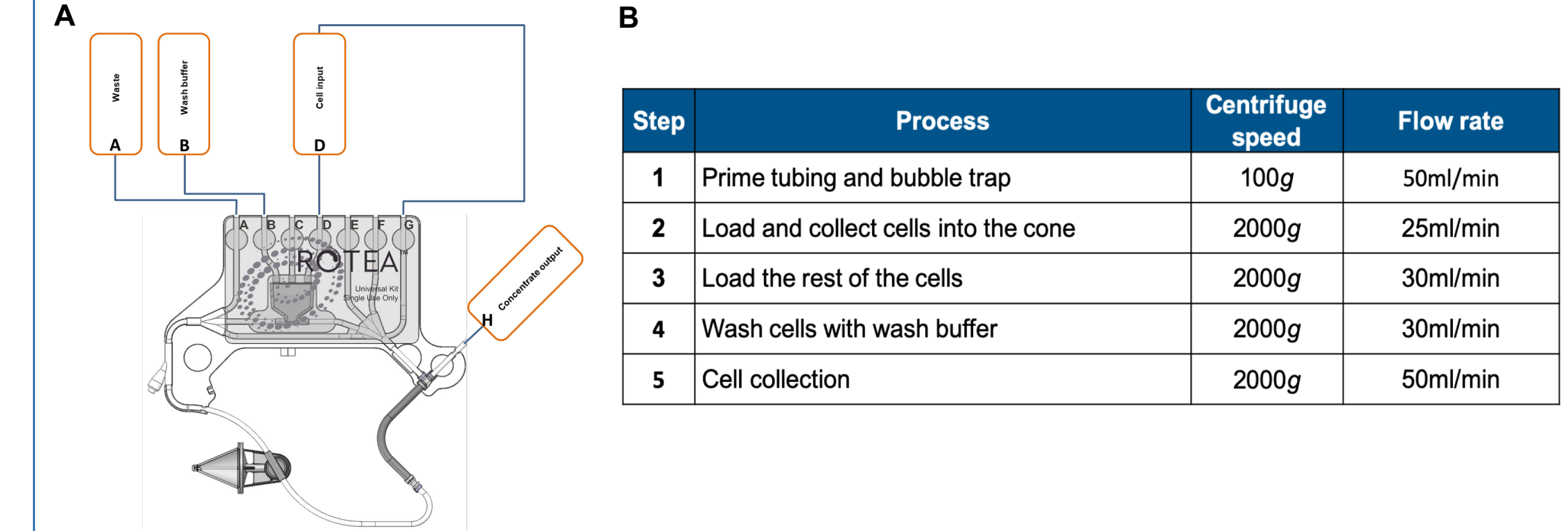


Figure 6. Consumable setup and protocol for T cell wash and concentrate using Rotea. (A) Schematic diagram of Rotea single-use kit connecting with bags for input, output, and buffers. (B) Automated steps for Rotea T cell wash and concentrate.

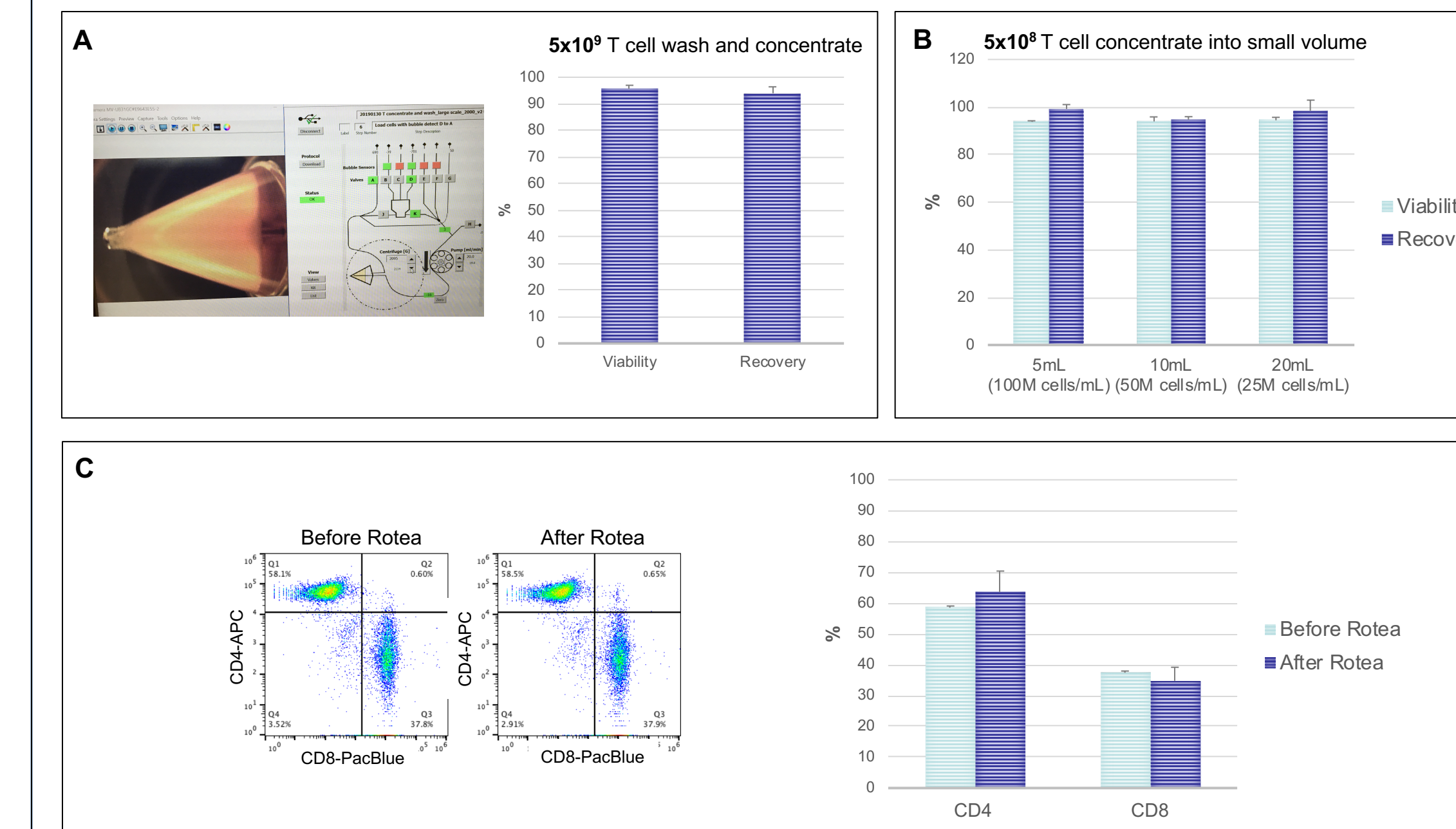


Figure 7. T cell wash and concentrate with controllable input and output scales. (A) Rotea chamber (left) accommodates more than 5×10^9 T cells, and maintains high viability and recovery after wash. (B) Rotea precisely controls output volume as low as 5mL or less, therefore provides cell concentration as high as 1×10^8 cells/mL in the output collection. (C) T cell composition remain the same after Rotea wash and concentrate.

CONCLUSIONS

- Rotea provides highly efficient PBMC isolation with high recovery and superior cell quality as compared to Ficoll separation.
- Rotea provides gentle and efficient cell wash and concentrate with flexible input and output volume.
- Rotea facilitates the whole cell therapy workflow from PBMC isolation all the way to cryopreservation.

TRADEMARKS/LICENSING

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