

# Optimizing Cell Sourcing for Cell Therapy by Reducing Donor Variability with Recallable Leukopak Donors for Enhanced Standardization

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## INTRODUCTION

Leukopaks are a blood-derived product containing a high concentration of white blood cells (WBC) (Figure 1), which is an invaluable starting material in cell therapies, such as CAR-T therapy, providing WBCs for research and development.<sup>1</sup>



FIGURE 1. Leukopak.

It is important to have cellular material from well-characterized donors and the option to obtain material from the same donor multiple times (recallable donors).<sup>2</sup>

This approach helps to reduce inherent variability between different donors and within the same donor over multiple donations.<sup>3</sup> By minimizing this variability, researchers may enhance process standardization, ensure reproducibility of results, improve preclinical studies reliability, and facilitate regulatory approval for new therapies (Figure 2).

## AIM

To assess the variability of leukopaks obtained from recallable donors and compare it against a total donor pool.

## METHODS

Data from six recallable donors with  $\geq 3$  donations over a 2-year time were analysed for intra-donor variability and compared against a total pool of donors. Leukopak parameters included WBC yield, distribution of each WBC subset (T cells, B cells, NK cells), and distribution of CD4+/CD8+ T cell ratio.

Variability in leukopak collections was expressed as mean coefficient of variation (CV), and categorized as low (<10%), medium (10-20%), or high (>20%).

The impact of process parameters on WBC yield was evaluated based on the ratio of Total Blood Volume (TBV) to Processed Blood Volume (PBV).

All leukopaks from the evaluated recallable donors exhibited TBV/PBV ratios ranging from 0.9 to 1.6, indicating minor variations in process parameters.

## RESULTS

Intra-donor variability in WBC yield was observed across all donors. Despite inherent variability, WBC yields within the same donor were lower (CV mean 15%, n=6) than the total donor pool (CV 25%) (Figure 3A).

WBC subsets also showed low-medium variability within each donor's donation (Figure 3B). Intra-donor variability ranged from 1.12% to 9.15% for T cells, 0.54% to 11.88% for B cells and, 2.77% to 16.86% for NK cells, indicating a consistent WBC subset distribution. Instead, the inter-donor variability of the total donor pool were all significantly higher (CV 12.51% for T cells, 30.40% for B cells and 51.58% for NK cells).

All CD4+ and CD8+ T cell distributions exhibited low variability within donors (CV range 0.45% to 3.39% for CD4+; CV range 0.39% to 3.45% for CD8+) (Figure 3C).

Instead, a notable variability was observed in the total donor pool (CV 13% for CD4+ and 23% for CD8+ T cells).

These results were aligned with demographic-associated alterations in immune T cells, among other variables.

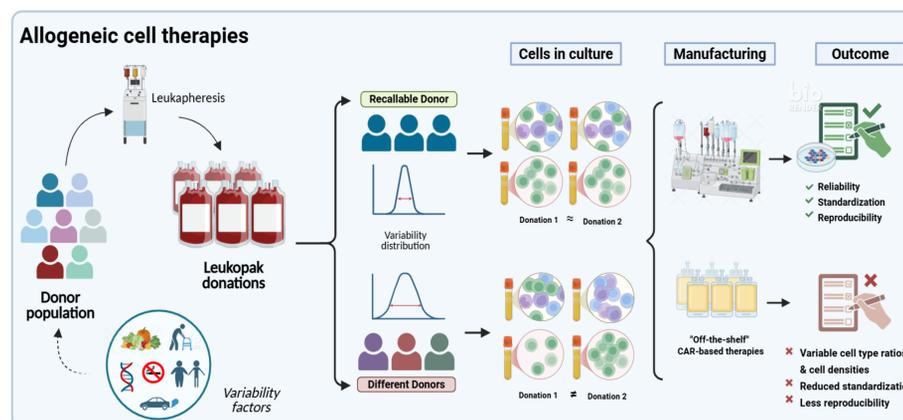


FIGURE 2. Comparison of outcomes in allogeneic cell therapies based on cell material sourcing from recallable donors versus different donors, highlighting the impact of donor variability.

## CONCLUSION

This study showed that using leukopaks from recallable donors helps to **reduce variability** in leukopak collections, **enhances standardization** and improves the **reliability** of preclinical studies.

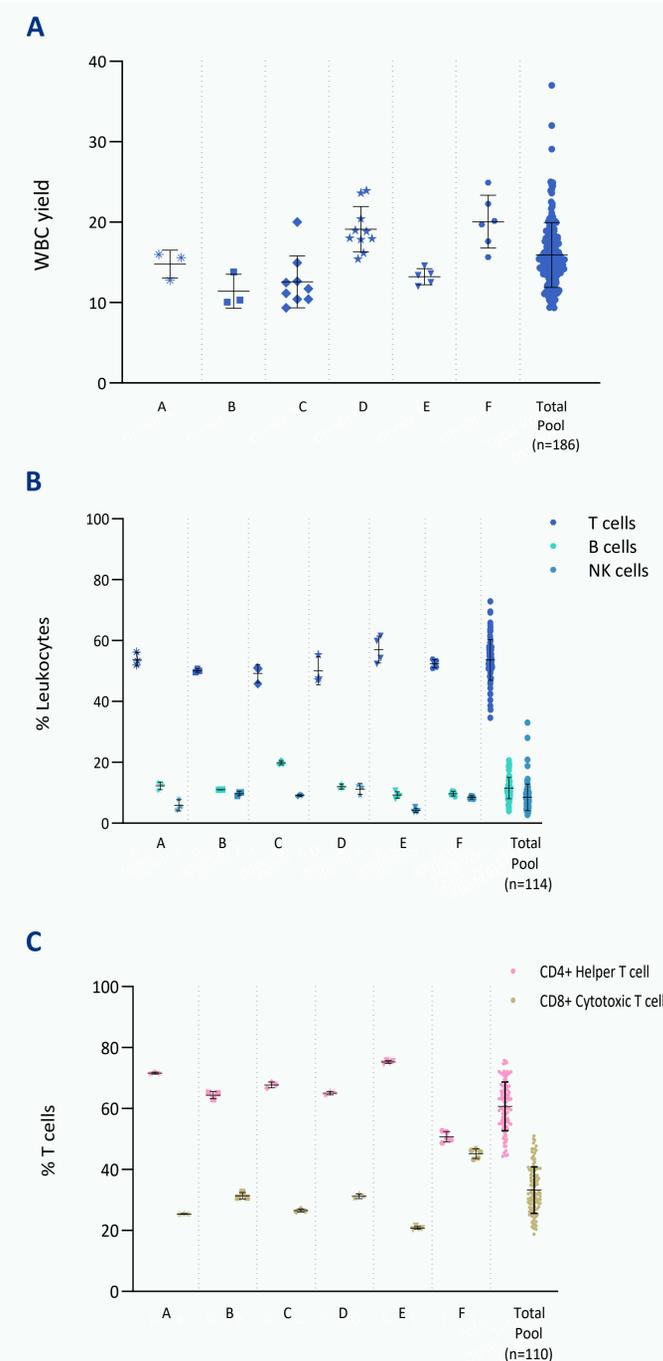


FIGURE 3. Intra-donor variability from multiple collections of recallable donors (1 to 6) compared to the total donor pool.

A) WBC yield. B) T cells, B cells and NK cells distribution. C) CD4+ Helper T cells and CD8+ Cytotoxic T cells distribution. Results are expressed as mean and SD.

## REFERENCES

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