Enrichment of T cells and T cell subsets by depletion of other cell types: An effective system to get to the clinic

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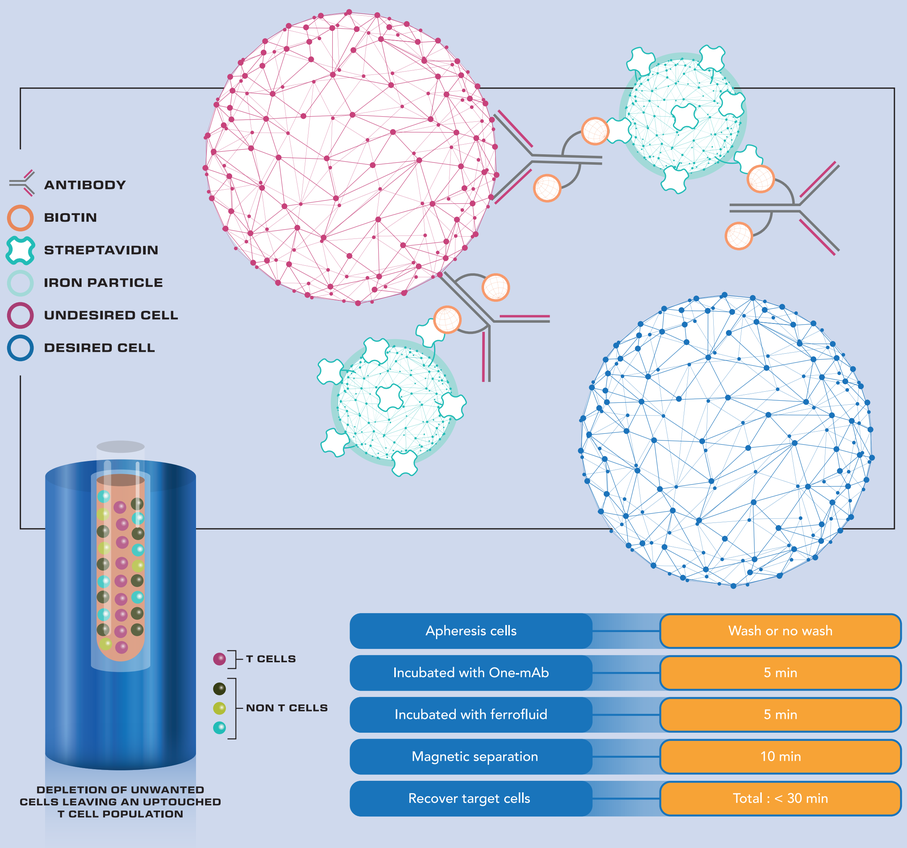
Abstract

Isolation of untouched T cells has long been in demand for clinical immune therapy but has largely been unavailable due to its complexity and the very high cost related to the number of monoclonal antibodies (mAbs) required. Here we present a strategy to enrich untouched T cells by removing unwanted cell types through the use of a single biotinylated monoclonal antibody. This is accomplished by inventively combining the functions of the binding capacity of both the mAb's Fab and Fc regions. Cells coated with the mAb can be captured using highly magnetic particles conjugated with streptavidin. Using fresh apheresis products, an enrichment of $CD3^+$ cells to 95 ± 3%, was achieved, these being at least 98% viable. The yield of T cells was in the range of 75 ± 10%. The process is fully scalable from the Quadrupole magnets designed for small scale laboratory benchwork through to the FerroSelect™ Array closed automated device designed for use with a full size leukopack. Moreover, by adding a second antibody to the above depletion process such as either an anti-CD4 or anti-CD8 mAb, $CD8^+$ or $CD4^+$ cells, respectively, can be enriched in an untouched state. In summary, this novel system (patent pending) is simple, economical, and rapid, and provides significant advantages for clinical applications in step with the rapid expansion of immune therapy.

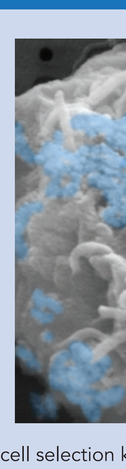
1 Principle and procedure of negative depletion



Apheresis cells	Wash or no wash
Incubated with One-mAb	5 min
Incubated with ferrofluid	5 min
Magnetic separation	10 min
Recover target cells	Total : < 30 min

2 FerroSelect™ ferrofluids

- Streptavidin ferrofluids
  - 130 - 190 nm in size with a high magnetic moment
  - No need to remove after processing, no costly columns
- Ready for the clinic
  - Manufactured with a recombinant human serum albumin coating and labeled with recombinant streptavidin: fully xeno-free with no animal origin components
  - The high magnetic moment of the particle combined with a planar magnet array allow for the capture of high numbers of cells
- A scalable technology to perform either simple positive selection or negative depletions of different cell types
- Streptavidin ferrofluid is available either as part of our own cell selection kits or as a stand-alone reagent for use with your own biotinylated mAb

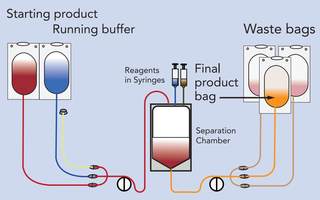


3 Equipment

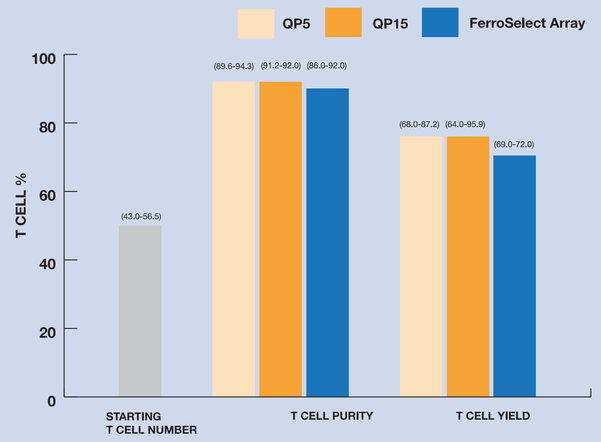
Handheld quadrupole magnets for processing 4.0 or 12.0 ml of cell suspension

FerroSelect Array instrument for processing either a ¼ or full size leucopak

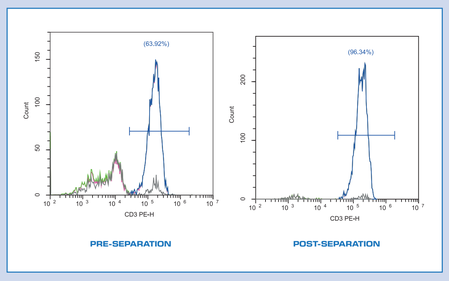
Disposable set



4 T cell selection: Scalability of CD3+ cell enrichment by depleting unwanted cell types.



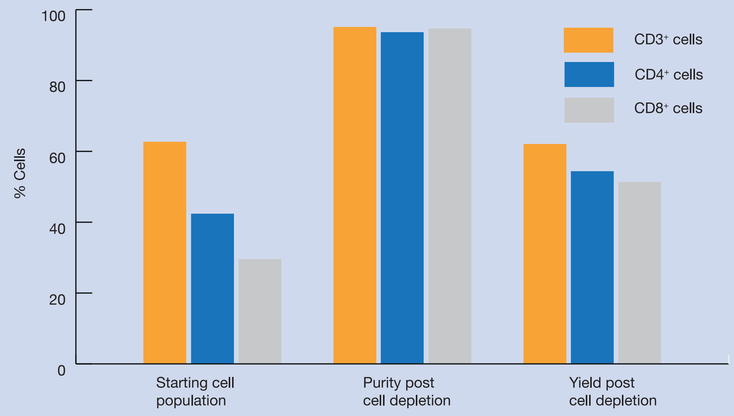
5 Cell subset analysis: T cell enrichment pre- and post-depletion



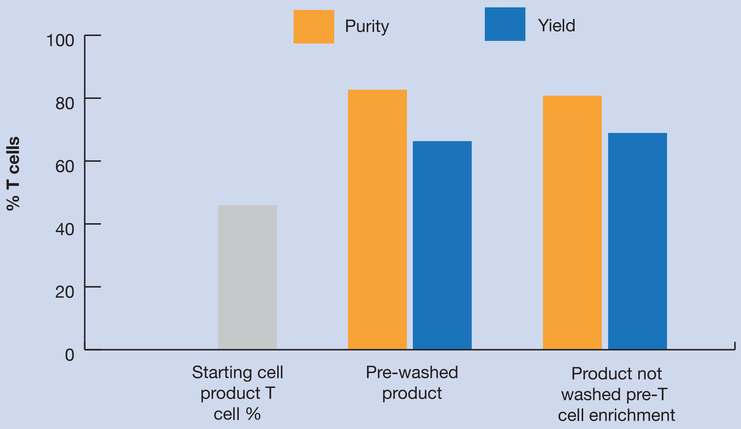
Cell subset	Pre %	Post %
T-cells	56.8	94.2
Mo/MØ*	21.0	1.3
B-cells	12.6	0.4
NK-cells	6.9	5.1

*Monocytes/macrophages

6 Enrichment of CD4 and CD8 T cell subsets by depletion of other cell types



7 High levels of T cell enrichment can be achieved without washing the apheresis product prior to depletion



Summary

An innovative cell selection system allowing for the enrichment of different cell types through the depletion of unwanted cells is described. The approach is simple, efficient, quick and economical and can provide untouched immune cells of various cell types for further processing as desired.

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