

Simply magnetic

FerroSelect™: designed to simplify selection and enrichment of your clinically important cells

Simply scalable
Simply reproducible
Simply accessible

Cell selection, **simplified!**

It's time to update your magnetic cell selection strategy. Competitive magnetic sorting technologies are a compromise requiring either large beads to provide sufficient magnetic force to capture cells, or an expensive and inefficient column to amplify the magnetic field to attract smaller, less magnetic particles. With BioMagnetic Solutions, you don't need to compromise.

Introducing FerroSelect™ ferrofluids, kits, and equipment:

- Highly magnetic ferrofluid particles assure high efficiency cell capture
- No particle removal needed after selection
- No requirements to wash out reagents between incubations
- Novel AbsenT™ negative depletion antibody technology for collecting untouched cells
- The FerroSelect Array manufacturing platform streamlines and automates your cell selection capabilities
- Designed for tomorrow, ready today

Isolation or enrichment of cells using our core ferrofluids

Our unique ferrofluids are designed to provide consistent purification of desired cells from complex mixtures such as peripheral blood or leukopaks. When combined with our optimized FerroSelect biotinylated antibodies, you can expect quick and easy retrieval of your cells of interest, using either our quadrupole magnets or our FerroSelect Array closed, automated, planar magnetic system designed for manufacturing.

Our ferrofluid nanoparticles:

- Are optimized with a nominal size distribution centered at 150 nm, avoiding steric limitations of micron-sized magnetic beads used in some competitive systems, and permitting filter sterilization
- Cells coated with magnetic particles can be captured on a planar magnet radically simplifying the collection process and eliminating the need for column requiring equipment
- Use only GMP-grade recombinant materials (e.g. human serum albumin (HSA), and streptavidin) to assure consistency and avoid introducing animal components
- Are compatible with cGMP manufacturing processes

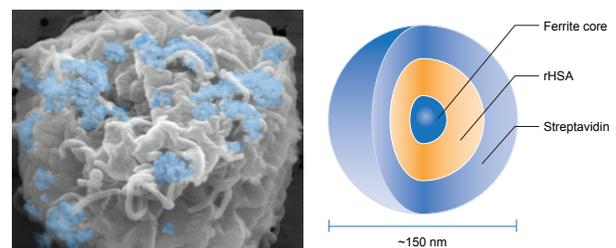


Figure 1: Electromicrograph of ferrofluids attached to a T cell via the CD3 receptor.

Our ferrofluids are either provided within FerroSelect kits, or separately in three sizes to allow experimentation with your own biotinylated antibodies:

- One small vial supports the selection of approximately 1.2×10^8 cells
- One medium vial supports the selection of approximately 2.0×10^9 cells
- One large vial supports the selection of approximately 8.0×10^9 cells

Develop your ferrofluid cell selection processes with one of our easy to use FerroSelect quadrupole magnets

Our quadrupole (QP) neodymium iron boron rare earth magnets are engineered to capture ferrofluid labeled cells without the use of expensive and inefficient capture columns. These devices allow you to optimize experimental conditions in your lab before scaling up onto our FerroSelect Array closed manufacturing platform.



FerroSelect QP5

For processing volumes up to 4.0 mL (8×10^7 cells in a 12 x 75 mm tube)



FerroSelect QP15

For processing volumes up to 12.0 mL (2.4×10^8 cells in a 17 x 120 mm tube)

Key Features & Benefits

- High strength handheld quadrupole magnets are designed for lab scale cell separations letting you test and optimize experimental conditions prior to scaling up to larger systems such as our FerroSelect Array closed automated platform
- Perfectly matched to our FerroSelect reagents allowing you to purify your cells of interest without the use of expensive equipment or devices requiring column-based magnetics

Our FerroSelect Array automates large-scale cell selection in a simple, single-use format

We designed the FerroSelect Array to address many of the shortcomings of existing cell selection platforms. Developed from the ground up to take advantage of our proprietary array of neodymium iron boron rare earth magnets the instrument enables bulk collection of cells directly from either a quarter or full leukopak.

The FerroSelect Array fully-automated, closed, single-use cell selection platform brings high-volume cell capture to your benchtop. When used with our variety of positive and negative selection kits, cellular subsets are quickly and easily isolated from leukopaks or other cell sources.

Key Features & Benefits

- Single-use consumable assures trouble-free processing
- Includes validated cell selection and depletion protocols optimized for use with FerroSelect reagents
- User programmable with quick setup, operation, and cleanup providing complete flexibility to optimize your experimental methods

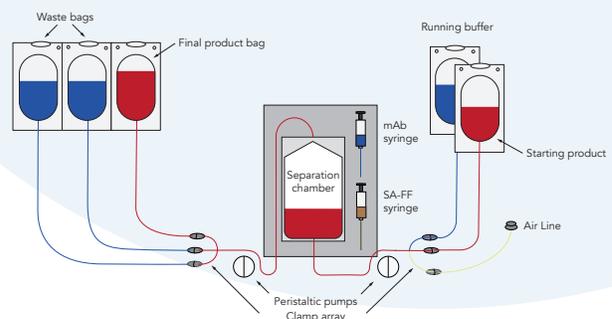


Figure 2: The FerroSelect Array is designed to complement the capabilities of the platform and let you quickly setup and execute either a pre-programmed or customized selection procedure using a single-use sterile consumable.

Simplify your positive cell isolation with our cell selection kits and reagents

Our positive selection reagents are designed to enable quick and efficient cell separation from virtually any sample type using our antibodies (or developing your own protocols with third party biotinylated antibodies). Following a brief incubation period, as short as 5 minutes, cells can be collected from the cell suspension using either our FerroSelect QP magnets or our FerroSelect Array platform.

We currently offer CD3⁺, CD4⁺, CD8⁺ cell selection kits, and more are on the way!

Check www.biomagneticsolutions.com for current availability.

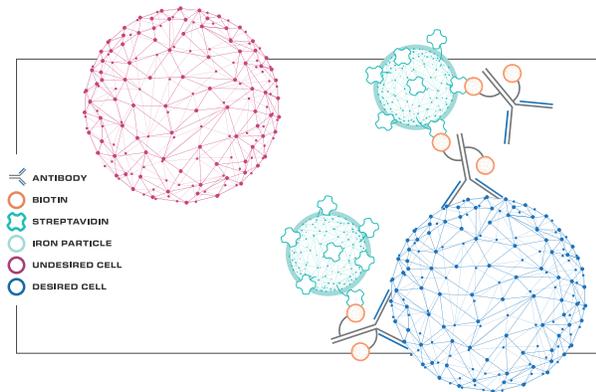


Figure 3: Positive cell selection involves attaching ferrofluid particles to desired cells while avoiding non-specific binding to undesired cells. Our fully recombinant and xeno-free technology affords high specificity and efficiency in cell selection procedures.

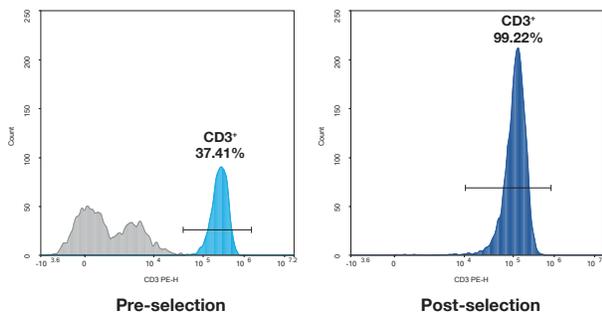


Figure 4: Selection of CD3⁺ (T cells) using a quadrupole magnet.

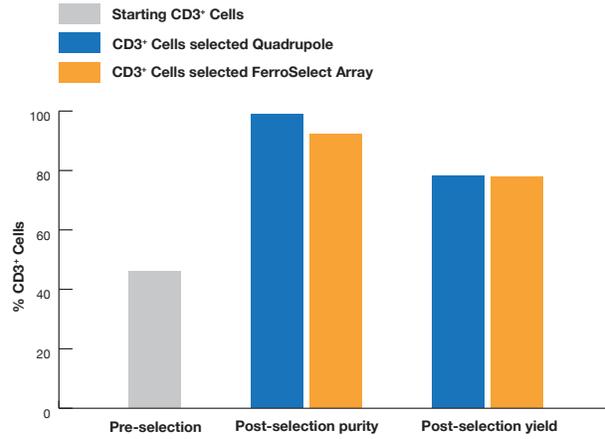


Figure 5: Positive cell selection of CD3⁺ cells from a fresh leukopak of human cells using either a QP5 Quadrupole magnet or the FerroSelect Array.

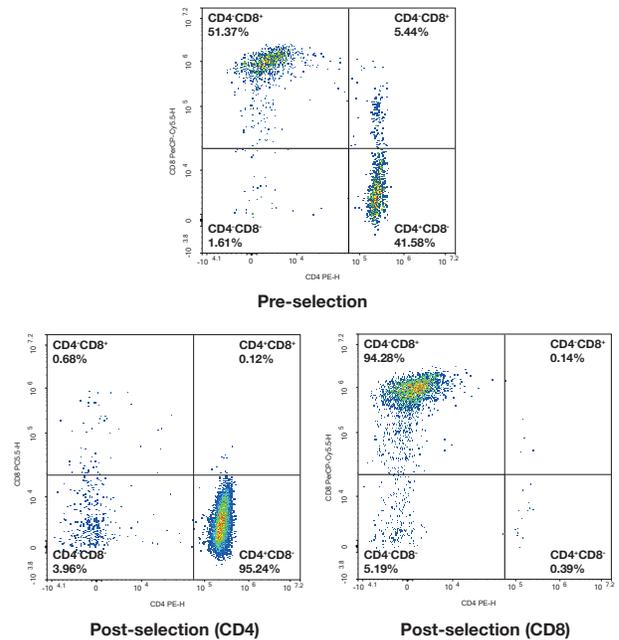


Figure 6: Positive selection of either CD4⁺ or CD8⁺ cells from a fresh leukopak of human cells using our CD4⁺ and CD8⁺ reagent kits.

FerroSelect AbsenT untouched cell enrichment is possible with only one or two antibodies

Many cell therapy manufacturing applications benefit from negative cell depletion methods which leave a highly enriched population of desired cells, without the concern of interfering reagents persisting in subsequent processing steps. We have developed (patent pending) a novel approach that uses as little as one or two antibody specificities to accomplish what competing platforms can only do with 6 or more. Using combinations of either one or two antibodies, we can provide untouched subpopulations of T cells (CD3⁺), effector/ cytotoxic T cells (CD8⁺), helper T cells (CD4⁺), and plan to launch additional products in the AbsenT line in the future.

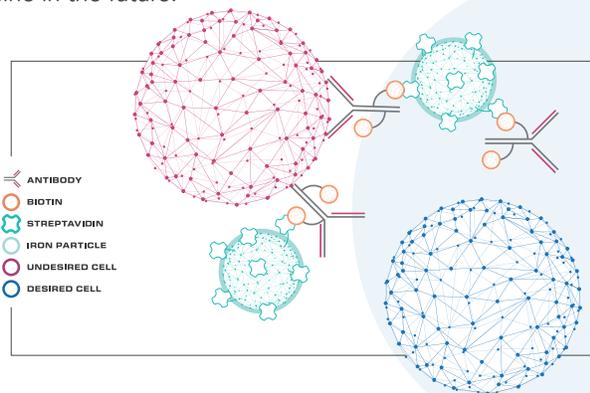


Figure 7: Schematic diagram of AbsenT cell depletion leaving a highly enriched population of untouched cells of interest

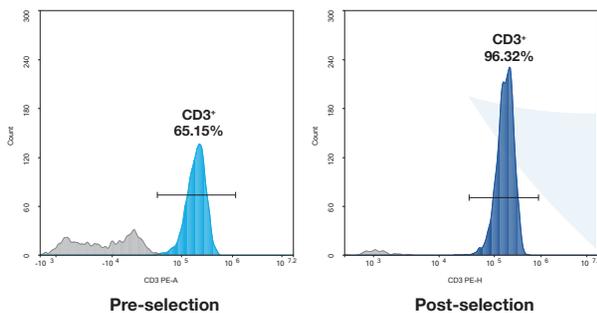


Figure 8: Histograms from a CD3⁺ cell enrichment performed by depleting other cell types using FerroSelect AbsenT depletion reagents and a Quadrupole QP5 magnet.

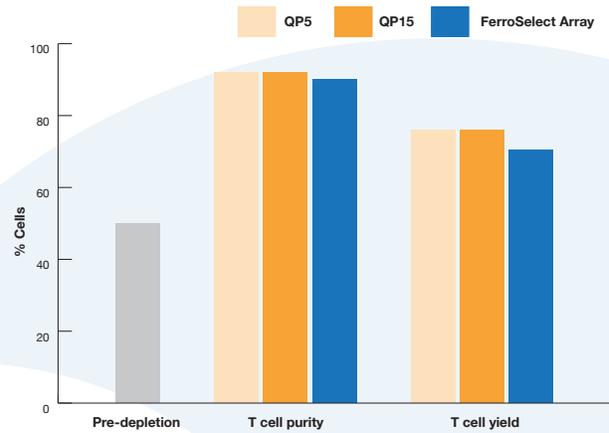


Figure 9: Negative depletion of unwanted cells using both our FerroSelect QP5 and our FerroSelect Array, demonstrating the comparability between the hand-held open magnet and the closed, automated FerroSelect Array

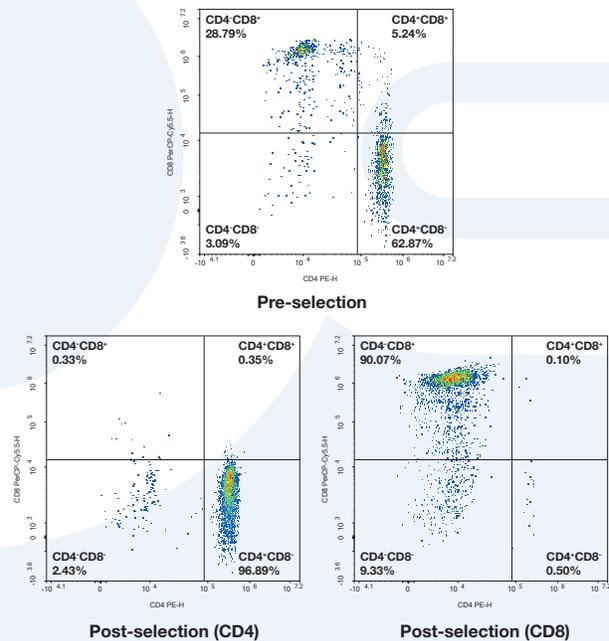


Figure 10: Enrichment of T cell subsets following the depletion of unwanted cells using our FerroSelect AbsenT Selection kits for CD4⁺ and CD8⁺ cells.

Tunable T cell activation & expansion in a single step

Expansion of T cells requires a stimulatory event, typically triggered *ex vivo* by activating cells via their CD3 and CD28 receptors. Clustering of T cell receptors is accomplished by complexing our FerroSelect ferrofluids together with biotinylated anti-CD3 and anti-CD28 antibodies. Artificial cross-linking of the receptors and/or three-dimensional changes of the receptor complex initiates a signaling cascade driving cells into division and concomitant cytokine release. Artificially adding Interleukin-2 (IL-2) further drives T cells into activation and division.

Activation can be achieved:

- Following **positive selection** of T cells using our FerroSelect ferrofluids, anti-CD28 antibody and IL-2 added directly to the cell culture drives T cell activation and subsequent cell division, or;
- Following **enrichment** of T cells using our AbsenT Depletion kit the T cell activation reagents are simply incubated with the untouched cells in culture and serve as the receptor clustering agent.

In both examples the activation and the expansion of T cells can be optimized by using different quantities and ratios of anti-CD3 / CD28 antibodies – a unique feature of the FerroSelect system.

Key Features & Benefits

- Activation and expansion can be optimized by titrating the various reagents to meet experimental needs
- By day 7 neither biotinylated antibodies nor streptavidin ferrofluid can be identified on the surface of T cells by flow cytometry
- Re-stimulation using the FerroSelect CD28 kit is possible to further drive cells into activation and division

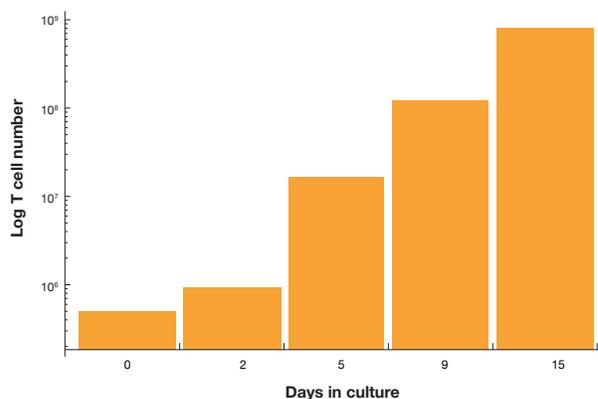


Figure 12: Expansion of T cells following their selection using the FerroSelect CD3⁺ Kit. T cells were seeded at 5×10^5 cells per ml in the presence of 1.5 $\mu\text{g/ml}$ of anti-CD28 and 10.0 ng/ml of IL-2.

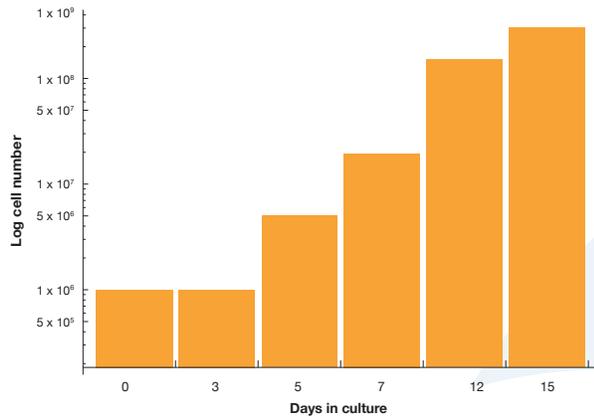


Figure 13: Expansion of T cells following their enrichment by depleting unwanted cells using the AbsenT CD3⁺ Kit. Cells were seeded at 5 x 10⁵ cells per ml in the presence of 1.5 ug/ml of anti-CD28, 1.5 ug/ml of anti-CD3, 10.0 ug/ml of streptavidin ferrofluid and 10.0ng/ml of IL-2.

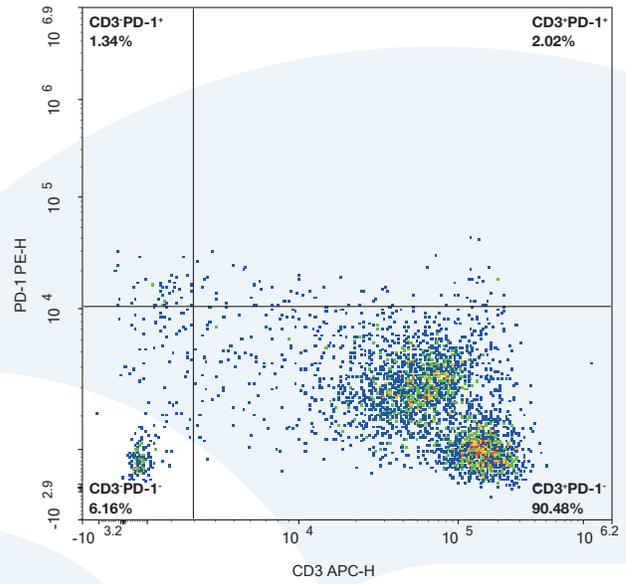


Figure 15: Low level PD-1 expression on cells cultured with biotinylated anti-CD3, anti-CD28 and streptavidin ferrofluid on day15 of culture. Low levels of the surrogate marker are indicative of their ability to activate in the presence of appropriate stimuli.

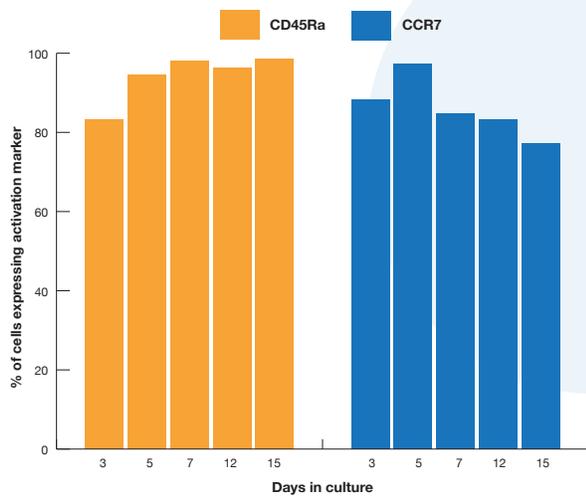


Figure 14: Maintenance of the naive state of T cells following their activation and expansion. T cells were enriched using the AbsenT kit and expanded using the conditions detailed above. The naive status of the T cells over the period of activation/expansion was determined by the surrogate markers CD45Ra and CCR7.

KITS:

Product Name	Description	SKU
Hardware		
FerroSelect QP5	Handheld quadrupole neodymium iron boron magnet designed for use with FerroSelect reagent kits for cell separation volumes up to 4.0 mL.	24-0001
FerroSelect QP15	Handheld quadrupole neodymium iron boron magnet designed for use with FerroSelect Reagent Kits for cell separation volumes up to 12.0 mL.	24-0002
FerroSelect Array	A functionally closed, fully automated & programable instrument for magnetic cell selection.	24-0003
Ferrofluids		
FerroSelect Ferrofluids	FerroSelect streptavidin ferrofluids for use with FerroSelect kits, hardware and other reagents, or with 3rd party sourced biotinylated antibodies.	28-0027 28-0028 28-0029
Reagent Kits		
FerroSelect CD3 Kit	Contains biotinylated anti-CD3 and streptavidin ferrofluid. Optimized for rapid positive selection of CD3 human T cells with our hardware.	28-0003* 28-0002* 28-0001*
FerroSelect CD4 Kit	Contains biotinylated anti-CD4 and streptavidin ferrofluid. Optimized for rapid positive selection of CD4 human T cells with our hardware.	28-0019* 28-0023* 28-0024*
FerroSelect CD8 Kit	Contains biotinylated anti-CD8 and streptavidin ferrofluid. Optimized for rapid positive selection of CD8 human T cells with our hardware.	28-0021* 28-0025* 28-0026*
FerroSelect AbsenT CD3 Kit	For negative depletion and enrichment of untouched CD3 T cells. Contains a biotinylated monoclonal antibody and streptavidin ferrofluid. Optimized to enrich CD3 human T cells with our hardware.	28-0009* 28-0008* 28-0007*
FerroSelect AbsenT CD4 Kit	For negative depletion & enrichment of untouched CD4 T cells. Contains a biotinylated monoclonal antibody, anti-CD8 and streptavidin ferrofluid. Optimized to enrich CD4 human T cells with our hardware.	28-0035* 28-0043* 28-0044*
FerroSelect AbsenT CD8 Kit	For negative depletion & enrichment of untouched CD4 T cells. Contains a biotinylated monoclonal antibody, anti-CD4 and streptavidin ferrofluid. Optimized to enrich CD8 human T cells with our hardware.	28-0037* 28-0045* 28-0046*
FerroSelect CD3/CD28 Activation/Expansion Kit	For activation and expansion of T cells. Kit contains biotinylated anti-CD3, biotinylated anti-CD28 and streptavidin ferrofluid. Designed for the selection of CD3 human T cells followed by activation/expansion. May also be used to activate T cells enriched using FerroSelect AbsenT Kits.	28-0013* 28-0014* 28-0015*
Accessories		
FerroSelect Array Disposable Set [Sterile]	Single-use disposable is designed for use with FerroSelect Array, providing a convenient, biocompatible, and sterile fluid path for easily loading cells.	16-0001* 16-0002*
FerroSelect PBS	Base running buffer for enrichment performed by removing unwanted cells. Two volumes available.	14-0006 14-0008
FerroSelect PBS (Mg & Ca Free)	Base running buffer for positive selection. Two volumes available.	14-0005 14-0007

*Available in 5-packs. Visit www.biomagneticsolutions.com for more information.
All of our reagent kits are human specific.

Cell selection, **simplified!**



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