

# EFFECTIVE LEUKOCYTE ISOLATION WHITEPAPER

24-Jun-13

A Novel Flow Through Approach to Immuno-  
magnetic Cell Isolation

The BioCEP CEPir based on the patented Cell Enrichment Process enables effective isolation of cell populations with improved recovery, purity and viability in comparison to state of the art magnetic cell isolation technologies. In Leukocyte isolations the CEPir demonstrates increased purity of 6-33% and increased recovery rates of 8-19% over competing technologies.

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# Effective Leukocyte Isolation Whitepaper

## A NOVEL FLOW THROUGH APPROACH TO IMMUNO-MAGNETIC CELL ISOLATION

### IMMUNO-MAGNETIC CELL ISOLATION CHALLENGES

Cell population isolation has become common practice in research and development labs. Isolated cells are used in immunology, pharmacology, diagnosis and various therapies. Immuno-magnetic based cell separation techniques allow quicker isolations compared to flow cytometry technologies, and deal with higher specimen volumes. These technologies also offer the advantage of low capital investment in the isolation device.

Immuno-magnetic isolation, however, has a number of drawbacks which affect the quality of the isolated cells thereby affecting the downstream applications which can be performed with the isolated target cells. Additionally, this technology has not been found to be effective for isolation of rare cell populations.

The following is a list of common challenges associated with state-of-the-art cell isolation technologies:

- Cell abrasion which leads to cell clusters, lowering specimen purity, and to low viability of the cells
- Aridity of the specimen during plunging, lowering cell viability
- Volume limitations which prevent large-scale isolations
- Weak magnetic fields which hamper effective isolation of rare cells and sub-optimal purity levels of the separated specimen
- Low recovery rates

To overcome these challenges, cell isolation companies recommend rerunning isolations to receive the desired recovery rates and purity. This alternative is expensive and time-consuming and leads to decreased viability of the isolated cells

### THE CEPiR: FLOW THROUGH, MEDIUM FREE ISOLATION

Difficulties inherent in the current state-of-the-art separation technologies include weak magnetic fields, low capacity and little flexibility in configuration resulting in considerable damage to cells. BioCEP mitigates these difficulties by its Cell Enrichment Process (CEP) technology, a flow-through, contact free technology, that yields highly viable cells and exemplary purity of the isolated cells. Through user controlled magnetic field intensity and protocol definition, the CEPiR provides a level of isolation hitherto unavailable in state-of-the-art systems.

The CEPiR is specially designed to overcome drawbacks of the current state-of-the-art immuno-magnetic and flow cytometry technologies. The CEPiR represents a quantum leap in the design of

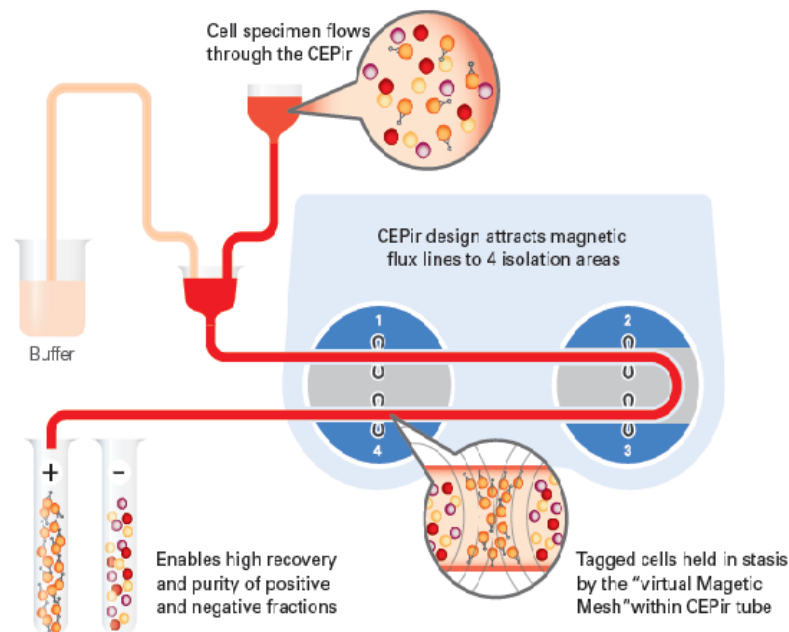


magnetic cell isolation/separation systems. Already patented globally, the CEP combines the flexibility and subtlety of continuous flow technology with efficacy of its unique “virtual magnetic mesh” design. The closed-circuit, virtual mesh completely eliminates the undesired contacts between cells and solid surfaces. Also unique to the CEPir are the continuous linear separation areas within the transport tubing that serves also as the separation vessel. The CEPir dramatically improves the yield of isolated cells with little or no change in their native morphology and viability.

The CEPir’s outstanding capabilities and features surpass by far those of the existing magnetic separation technologies. The CEPir separates cells with high purity and recovery; it can effectively separate cells as rare as one in a billion (incidence of  $1 \times 10^{-9}$ ). CEP isolated cells are suitable for downstream applications and analysis. This and other capabilities make the CEPir platform highly suitable for effective cell separation which will support the development of breakthrough applications which have suffered from lack of innovation due to the limitations of current technologies.

## THE CEP TECHNOLOGY

The CEP technology is based on a gentle, flow through design, electromagnets and a unique degaussing module. As the specimen flows through the CEP, tagged cells are held in stasis within the virtual mesh, eliminating surface contact with the targeted cells. Electromagnets create strong magnetic fields which enable rare cell isolation. The results are significantly higher yields of targeted cells with little or no change in their original morphology. The proprietary software allows parameter definition, such as, the intensity of the magnetic field, system capacity and separation time.



## ADVANTAGES ACHIEVED WITH THE CEPiR

### Increased Viability

Cells separated over the CEPiR, retain the original morphology. The CEPiR offers medium free isolation. The cells gently pass through the specialized tubing and are held in stasis in any of the four isolation areas. A buffer fluid is present throughout the process to prevent aridity. The CEPiR incorporates a gradual, novel process, for gentle collection of the positive fraction.

This approach prevents abrasion of cells preventing contaminating cell clusters and decreased viability. The novel design which maintains tagged cells in stasis ensures a cell-friendly environment. The gentle collection process prevents over-stimulation of the cells. The cells remain intact, with high viability, perfect for downstream applications.

CEPiR isolated cells retain their viability, reaching over 99%.



### Increased Recovery, After Only One Pass

The CEPiR's novel design comprises four isolation areas, each with a controllable magnetic field. The tagged cells flow through these isolation areas, and are held in stasis in any one of these. This approach quadruples the chances of successful isolation of the tagged cells, increasing the recovery rates of CEPiR isolations in comparison to existing technologies. The dialysis design and user-controlled software enable re-running isolations within the same kit, allowing virtually endless passes through the isolation areas for exceptional recovery rates.

Increased recovery translates into additional advantages such as higher viability, decreased time invested in isolations and lowers associated costs. It is this capability which enables the CEP to serve as an effective platform for rare cell isolation.

### Exceptional Purity

The unique design of the CEPiR isolation system ensures highly pure isolations, as tagged cells are held in stasis within the isolation areas and un-tagged cells flow through the system and out of it. As membranes remain intact, no cell aggregates, which are known to lower purity levels, form.

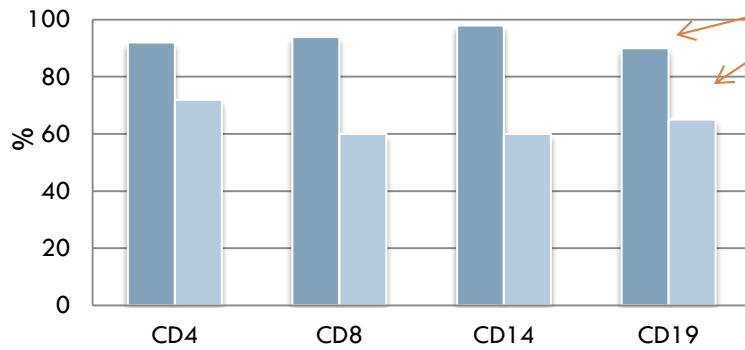
### Batch Isolations

As the CEPiR incorporates the best in flow through technologies it enables high volume isolations. A single run through the system can handle up to 50 ml and  $10^{10}$  tagged cells. The easy to use software system enables creation of protocols to handle multiple batches thereby increasing the total volume of specimen isolated 250 ml and more.

## LEUKOCYTES ISOLATION OVER THE CEPiR

The CEPiR is a significantly superior method for effective T-Cell isolation with superb recovery, viability and purity rates:

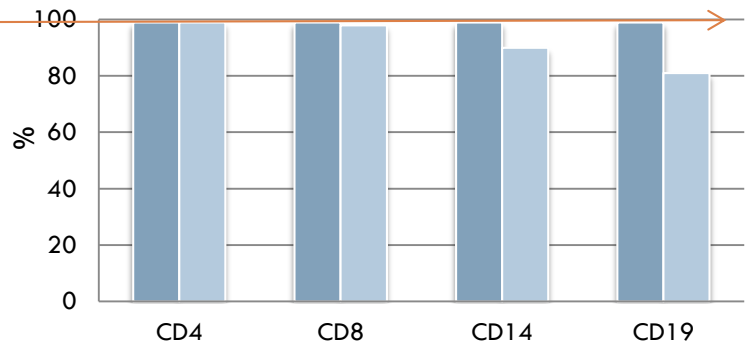
### Recovery after Single Isolation



Significantly higher recovery following a single pass through the CEPiR

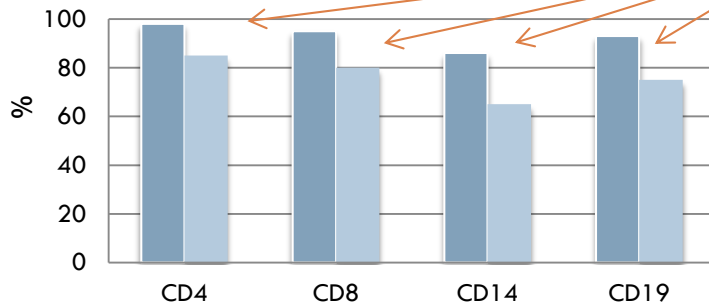
### Viability

Consistent >99% viability when using the CEPiR



### Purity

CEPiR ensures higher purity levels of cell isolations



Similar results were obtained in additional Leukocyte isolations such as CD 15, CD 3 and others.