

MiCareo

RARE CELL DIAGNOSTICS

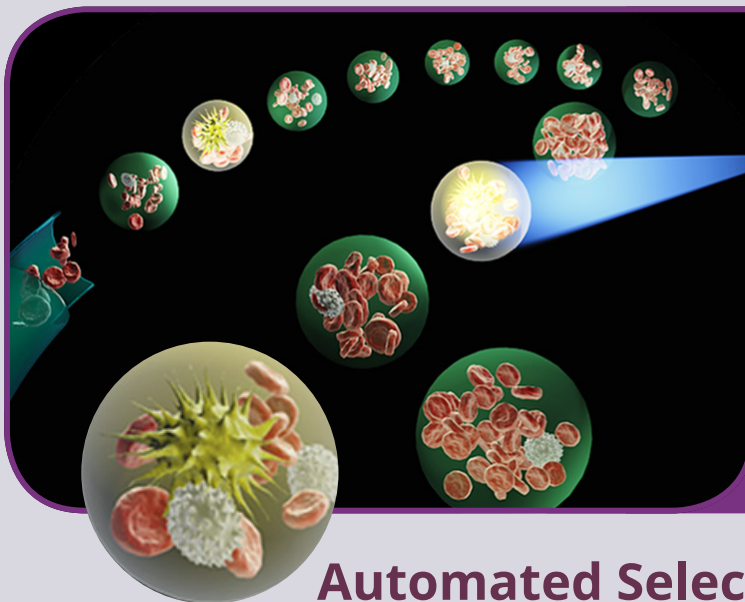


Unlocking the Secrets
of Rare Cells

Unlocking the Secrets of Rare Cells

MiCareo focuses on precision medicine and liquid biopsy technologies for rare cell isolation, including circulating tumor cells (CTCs) and immune cells. We are pushing beyond the limits of current liquid biopsy technologies to offer tools for drug developers and researchers to accelerate patient oriented drug correlations and biomarker discovery.

The potential applications of MiCareo's technology, when combined with researchers' willingness to explore new rare cells, is unlimited. We have developed excellent tools to light the way for precision medicine.



We capture, stain, and acquire high-dimensional fluorescent multiplexed images of rare cells.

From whole blood down to a single live cell.

Automated Selection of Rare Live Cells

The use of whole blood, in combination with MiSelect R's fully automated process – from cell selection to antibody labeling to fluorescence imaging – ensures that sample loss is minimized, and results are reproducible. Our gentle process and integrated instrument provide consistent access to isolated live rare cells such as CTCs and immune cells. The flexibility and downstream compatibility of our output improves the way pharmaceutical companies screen for drug effectiveness and allows researchers to find new correlations in biomarker expression.

Our unique imaging software transforms immune cell studies from the analysis of individual data points to a quantitative visual subtyping of each cell.

The MiSelect R Simply Solves Complex Problems

We have spent over a decade innovating an all-in-one system with a fully automated process that ensures that sample loss is minimized and results are reproducible. The Automated Microfluidic Sorting and Imaging System (MiSelect R) enriches and sorts rare cells using our patented ensemble-decision aliquot ranking (eDAR) process. The rare cells can also be retrieved for single cell studies or directly stained and imaged in our microfluidic chips.



Automated Microfluidic Sorting and Imaging System



Work Made Simple, Fast and Smart



Label whole blood

With minimal sample loss, and easier hands-on prep



Flexible marker panel

Choose our validated sorting reagents or your own cocktail



Let it run

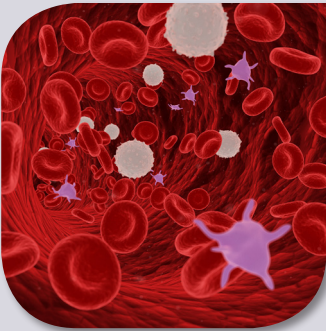
Automated process from enrichment to imaging



View the results

Watch your screen light up with a panel of target cells

Enrichment of Rare Cells – *From Billions to Thousands*



- Complex biological fluids containing billions of cells, such as whole blood, can be processed without using lysis or density centrifugation.
- Gentle preparation ensures minimal sample loss with less than 10% variation no matter who runs the sample.



- We label the whole blood containing the target cells with fluorescently tagged antibodies.
- Any cell surface antibody, or multiple antibodies, can be used.
- We don't use magnetic beads so there are no complicated conjugation steps.

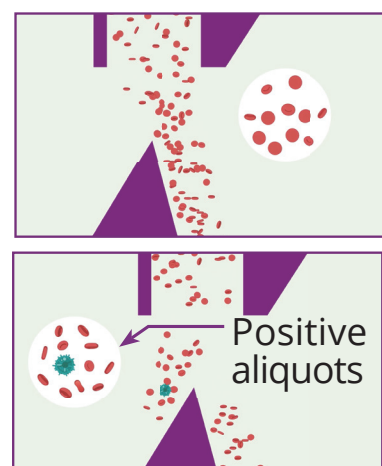


- To prevent contamination, the entire fluid pathway and our microfluidic SelectChips, are single use.
- Up to 16 mL of whole blood is processed quickly by using a laser to analyze nanoliter aliquots of the sample. Only those aliquots containing the target cells receive closer investigation.

Microfluidic processing sorts out the aliquots of blood that contain the target cells.

Each aliquot contains:
thousands of Red Blood Cells
15 to 35 White Blood Cells
1 Rare Target Cell.

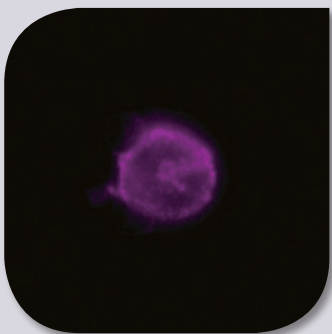
eDAR delivers single cell sensitivity even when starting with billions of cells.



Purification and Analysis – From Thousands to One

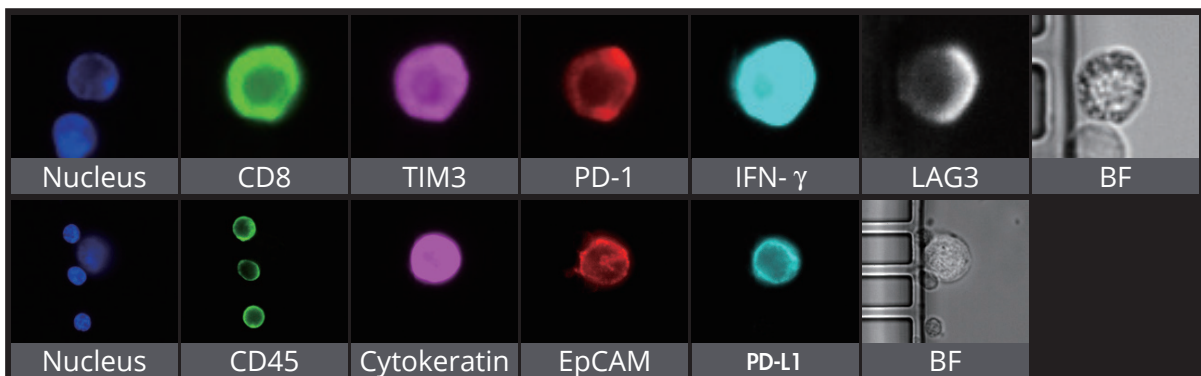
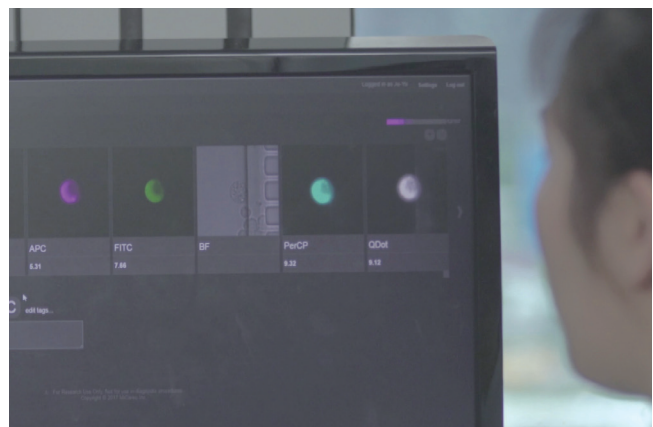


- The **SelectChip Dual** continues with on-chip purification using size-based filtration, which captures the nucleated cells.
- Only nanoliters are filtered, resulting in no clogging, cell shear stress, or capacitance issues, which are normally found with other technologies.



- The isolated individual cells are automatically incubated with up to **13** different antibodies.
- Fully integrated into the MiSelect R is a fluorescence microscope that records each cell.

- Included with our system is the AI machine learning cell analysis software **MiCyte**.
- **MiCyte** can gate the cells by fluorescence intensity, size, or morphology, and generate reports listing the different subtypes of cells.



SelectChip Retrieval - Cells for All Applications

The **SelectChip Retrieval** is designed to enrich rare cells and dispense them into a microcentrifuge tube with excellent recovery and high purity. The Retrieval chip skips the capture, labeling, and imaging steps found in the Dual chip.

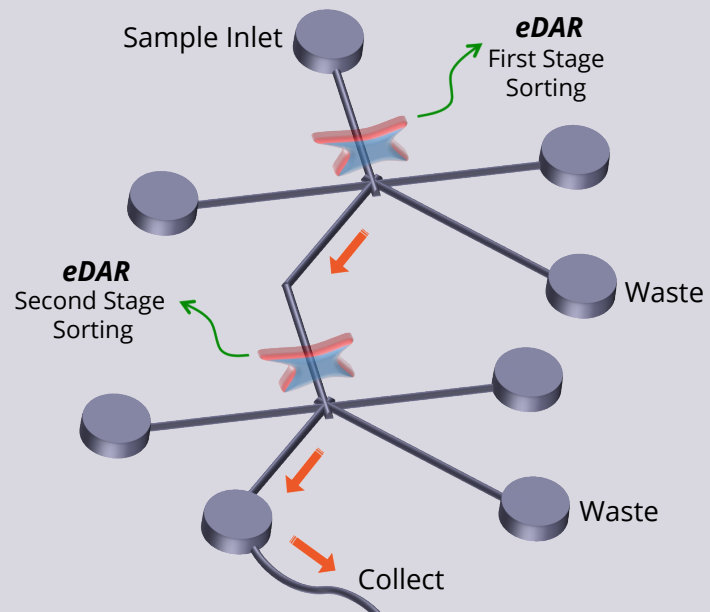
Two Stages of Sorting

for excellent cell purity.

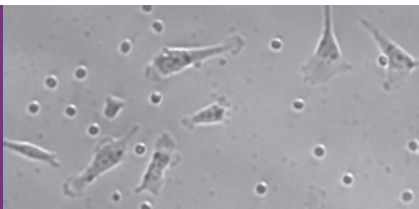
Example: 20 Target Cells
in 30 Million Nucleated Cells

After **eDAR** 1st stage:
18 Target Cells
600 Other Nucleated cells

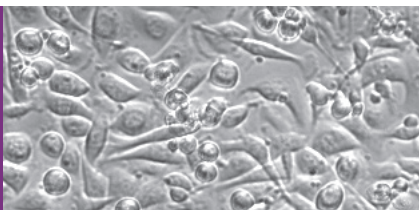
After **eDAR** 2nd stage:
17 Target Cells
20 Other Nucleated cells



Day 3



Day 9

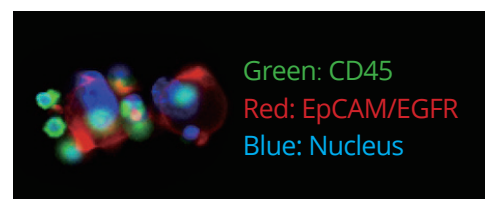
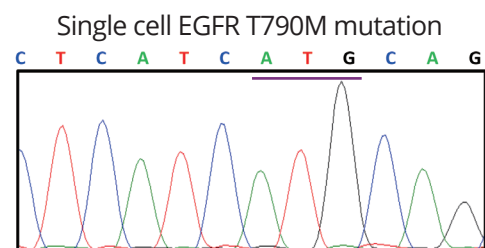


eDAR preserves the integrity of the cells with 99% survival, affording access to the complete range of genomic and cellular information.

The collected rare cells can be successfully cultured and exhibit an unchanged growth rate.

The high purity collected cells can be directly studied in bulk, or individually analyzed using single cell methods, such as sequencing for EGFR mutations.

The gentle fluid processing allows the sample to remain in a more natural state. For example, cancer cells can be observed interacting with immune cells.

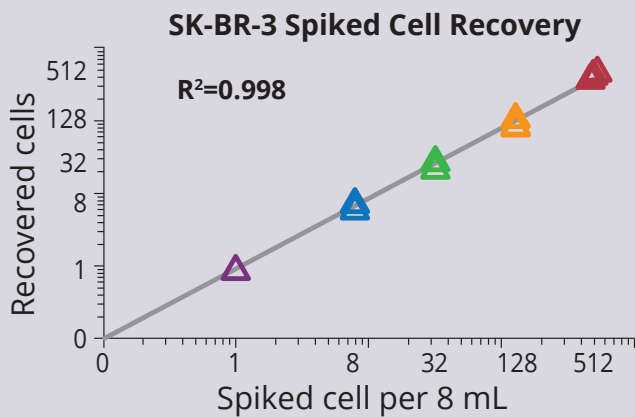


Reliable Results - With High Sensitive and Specificity

Even one single cell in 8 mL of blood can be found with greater than 97% sensitivity.

The automated labeling and imaging eliminates false positive cells.

		Cells Added to 8mL Blood			
		0	1	2	3
Cells Found in 8mL Blood	0	81	1	0	0
	1	0	46	1	0
	2	0	0	6	0
	3	0	0	0	17
Total Tests		81	47	7	17
Accuracy		100%	97.9%	85.7%	100%

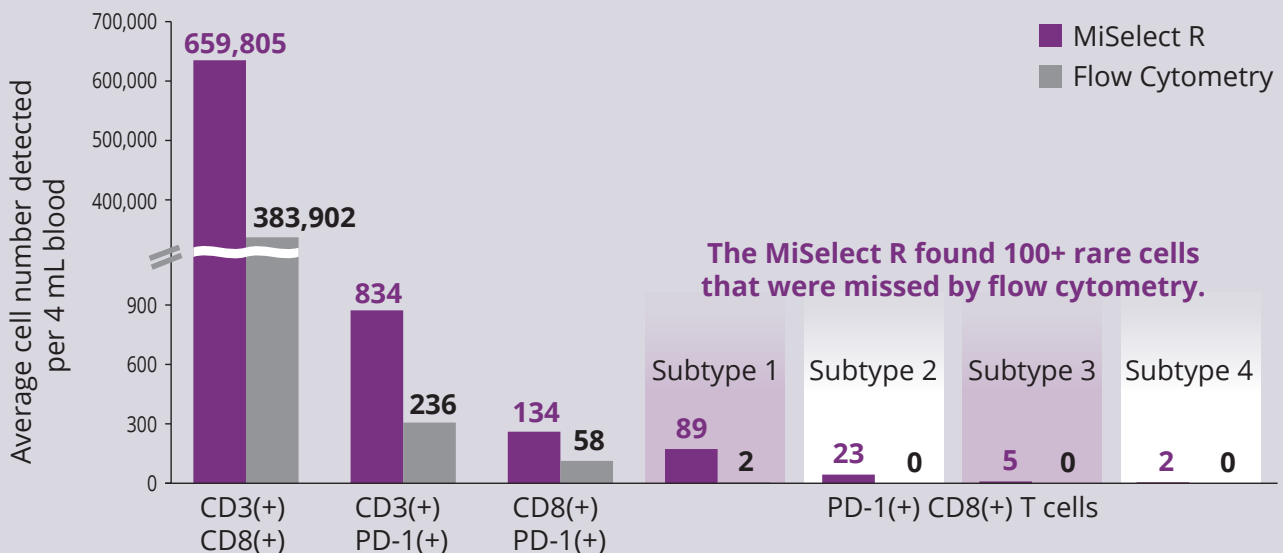


The MiSelect R with the SelectChip Dual achieves an average cell recovery of greater than 92%.

Best of all, users can confidently expect these results independent of operator experience level.

Flow cytometry is an excellent tool for cellular analysis, but quickly begins to fail when the target cells become a rare percentage of the total.

The MiSelect R allows for investigation of cell subtypes that flow cytometry simply cannot see.



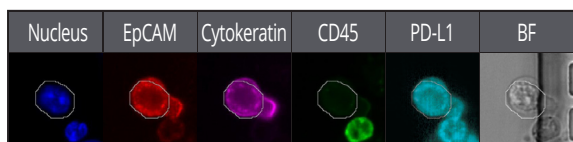
Actionable Clinical Results

The MiSelect R has been used to analyze more than 4,000 clinical samples including patients with breast, lung, kidney, liver, colorectal, urinary tract, and head and neck cancer. Sample types include blood, pleural effusion, cerebrospinal fluid, peritoneal cavity fluid, tumor tissue, and cells in suspension.

Two clinical examples highlight the benefits of automated selection, labeling, imaging, and analysis:

PD-L1(+) Circulating Tumor Cells

Blood was collected from colorectal cancer patients and analyzed for CTCs. The presence of PD-L1(+) CTCs was found to correlate with tumor staging, CEA, CA 19-9, blood and lymphovascular invasion. This example highlights the use of a blood test to evaluate potentially predictive cellular biomarkers.

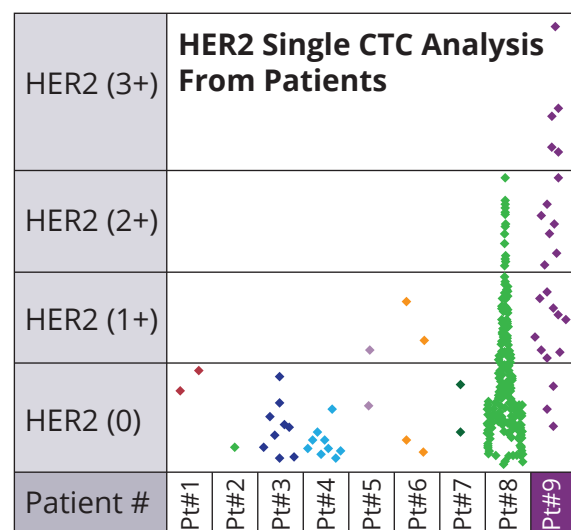


	Percentage of all patients with PD-L1(+) CTCs (N = 116)	Percentage of CTC positive patients with PD-L1(+) cells (N = 47)
Stage	8.3% (2/24)	40.0% (2/5)
Stage II	21.1% (8/38)	50.0% (8/16)
Stage III	35.7% (15/42)	78.9% (15/19)
Stage IV	50.0% (6/12)	85.7% (6/7)
P value	0.0017	0.0178

AACT 2018,78(13) Supplement: p.1589

Quantitative HER2 determination

Rapid and reproducible screening for HER2 level in breast cancer patients' peripheral blood is automated with the MiSelect R and the MiCyte analysis software. Preliminary results show that the HER2 status identified by CTC can be correlated with tumor biopsy immunohistochemistry HER2 results.



HER2 Testing CTC	HER2 Testing IHC	
	HER2 (+)	HER2 (-)
HER2 (+)	1/9	0/9
HER2 (-)	0/9	8/9

Powerful Cell Discovery

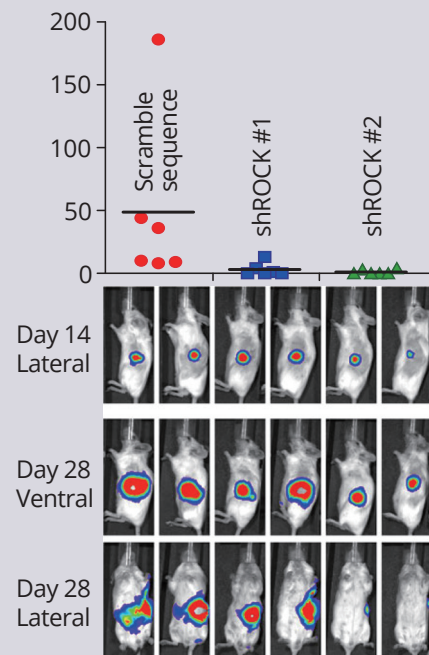
Thanks to the simple sample preparation, even small volumes of blood can be analyzed without cell loss.

For example, the MiSelect R has been used to track the dissemination of diffuse large B-cell lymphoma (DLBCL) in animal models.

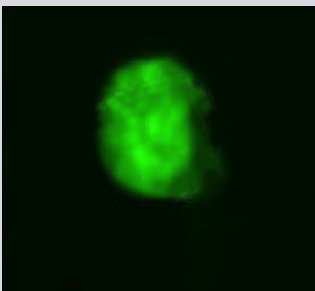
Beginning to understand the mechanism of DLBCL motility may explain the distinct clinical characteristics between patients with DLBCL and solid tumors and aids in the development of therapies tailored to patients' specific DLBCL clinical status.

Nature Communications volume 9, Article number: 3696 (2018)

Number of CTCs found

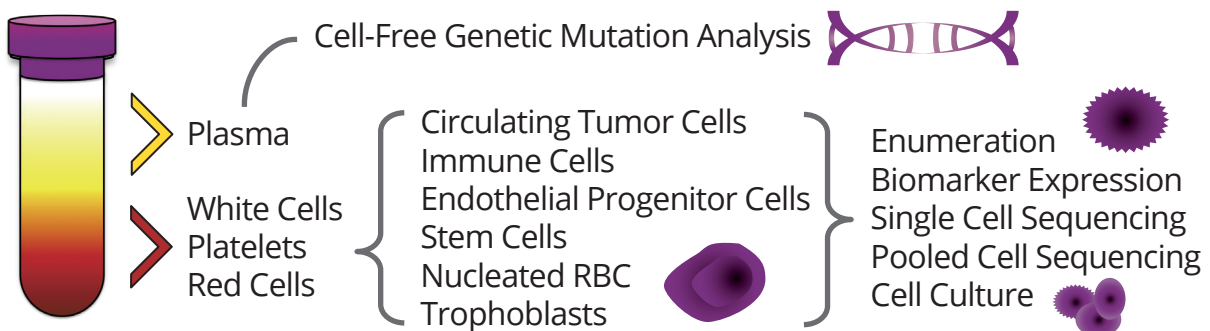


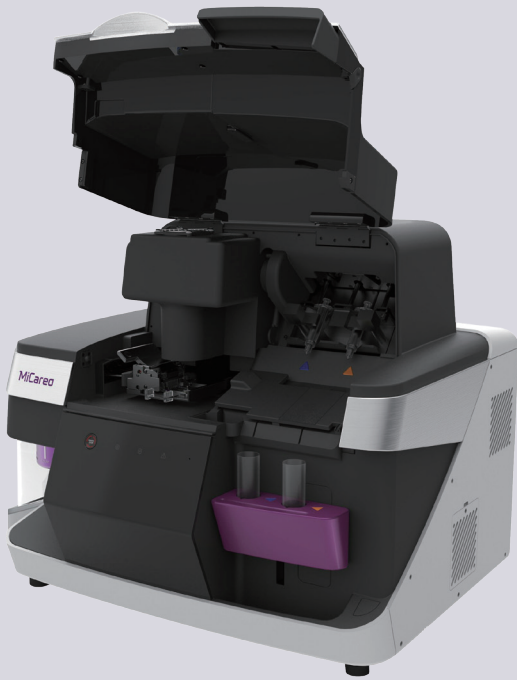
Natural Killer Cell



Cell therapy is a promising cancer treatment approach, but it is challenging to track the presence of rare active cells in patients after infusion. The high sensitivity of the MiSelect R makes it a unique tool for cell therapy monitoring for target cells such as CAR-T and natural killer cells.

Both cellular and cell-free plasma analysis can be performed with a single tube of blood.





MiSelect R

System Specification	
Size	70 cm (W) x 54 cm (H) x 53 cm (D)
Weight	78 kg
Sensor	High signal-to-noise ratio SiPM
Laser	Solid-state 488 nm, 50 mW
Camera	Scientific CMOS
Objective Lens	CFI Plan Apo Lambda 20 x 0.75 NA
LED Excitation	385 nm, 475 nm, 530 nm, 625 nm
Filter Flexibility	Seven replaceable imaging filters
Technologies	
Integrated fluorescence ranked cell sorting, size filtration, and imaging identification in one system	
Sample Type	
Whole blood, cell suspensions, and other fluids.	

Reagents

MiCareo has designed reagent kits for isolating CTCs and other rare cells for specific use with the MiSelect R platform. Use our validated SelectKit combination kits to sort and identify target cells or pick individual SelectSort and SelectProbe reagents to target your cells of interest. The MiSelect R can also accept any user supplied antibody.



Sorting Reagents

SelectSort EpCAM
 SelectSort EGFR
 SelectSort PD1

CTC Identification

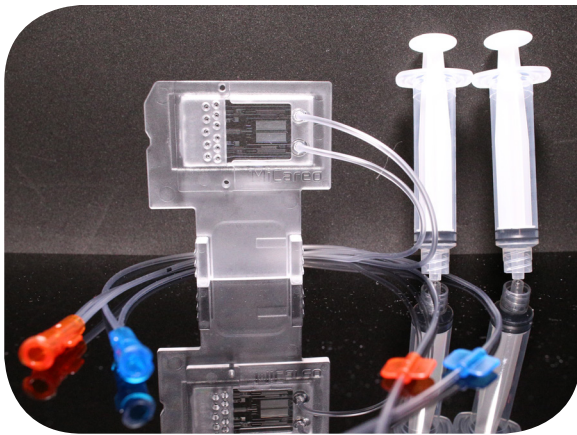
SelectProbe CTC
 SelectProbe CTC Plus HER2
 SelectProbe CTC Plus PD-L1

Kits for Sorting & Identification

SelectKit CTC
 SelectKit CTC EGFR Enhanced
 SelectKit CTC Plus HER2
 SelectKit CTC Plus PD-L1
 SelectKit Immuno PD1 Treg
 SelectKit Immuno PD1 CD8

SelectChip Dual – *Capture, Label, Image*

The SelectChip Dual is a single use microfluidic cartridge for isolating and imaging rare target cells from whole blood. Up to 13 biomarkers could be imaged on one single cell. The SelectChip Dual does not cause cell shear stress or capacitance issues normally associated with size based separation techniques.

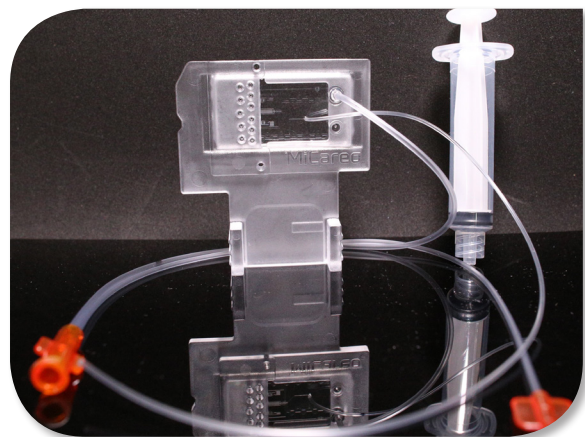


- Up to 16 mL of blood can be processed with a single chip.
- Dual channels for processing two samples at the same time.
- Thousands of small filter gaps and slow fluid flow gently captures even the smallest nucleated cells.

SelectChip Retrieval – *Select, Purify, Collect*

The SelectChip Retrieval is a single use microfluidic cartridge designed to enrich rare cells and output them into a small volume in a microcentrifuge tube or culture plate. The chip sorts whole blood and other fluids with high purity, allowing for direct coupling to many downstream analysis methods.

- Excellent recovery and high purity enrichment of live rare cells.
- Gentle processing and low shear stress maintain the integrity of the cells.
- Sort cells from 8 mL of blood in under two hours.



MiCareo Taiwan Co., Ltd.
5F, No. 69, Ln. 77, Xing Ai Rd., Neihu Dist.,
Taipei City 11494, Taiwan
Office: +886 2 2792 3976
Fax: +886 2 2791 9833
Taiwan toll-free number: 0800-606-288

MiCareo USA, LLC
Burlingame, California 94010, USA

Collaboration Service Center
Seattle, Washington, USA
Office: +1 650 918 6202

Info@MiCareo.com
www.MiCareo.com

Contact



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