MACS® Technology

One portfolio for all your cell isolation needs

MACS® Technology enables the magnetic separation of cell populations based on surface antigens. It is a fast and gentle method for the isolation of viable and functional cells by labeling epitopes with specific antibodies conjugated to superparamagnetic beads.

The MACS Technology portfolio provides a broad range of options for the isolation of virtually any cell type. Thereby, you enjoy the freedom to choose the cell isolation method that is best for your cells and your specific requirements. Our portfolio offers consistent, reliable cell separation solutions across basic and clinical research.

With MACS Technology, you are sure to select the best.

Starting material

**Single-cell suspensions**
- e.g. PBMCs, dissociated tissues (incl. tumors)
- MACS® MicroBeads
  - Columns
  - Nano-sized MicroBeads
  - UltraPure and REAlease™ MicroBeads

**Blood products**
- e.g. whole blood, buffy coat, apheresis products
- StraightFrom® MicroBeads
  - Columns
  - Nano-sized MicroBeads

**Positive selection**
- MACS Cell Isolation Kits
  - Columns
  - Nano-sized MicroBeads

**Untouched isolation**
- MACSxpress® Beads
  - Column-free
  - Micro-sized MACSxpress Beads
MACS® MicroBeads
See what makes MACS Technology the most-cited cell isolation technology.

See page 4

MACS® Columns
Learn about the advantages of MACS Columns – tested and trusted.

See page 5

The MACS® Technology advantage
Discover the advantage of using MACS MicroBeads and Columns.

See page 6

Cell separation
• Cell isolation from single-cell suspensions and dissociated tissues
• Cell isolation directly from blood products
• The next step in flexibility – label-free cells and challenging samples

See pages 7–9

Manual and automated cell isolation
Choose the right cell isolation method for your specific needs.

See page 10
MACS® MicroBeads – proven technology for basic research and clinical applications

MACS® MicroBeads are 50-nm superparamagnetic particles that are conjugated to highly specific antibodies against a particular cell surface antigen. Due to their small size, the beads do not activate cells. Furthermore, MACS MicroBeads do not have to be removed for any downstream application.

- MACS MicroBead Technology gives you the most flexible, most proven method for cell separation
- Minimal cell labeling with nano-sized MicroBeads ensures preservation of cellular integrity and characteristics
- Used in over 55,000 clinical cellular treatments to date

MACS MicroBead Technology owes its longstanding success to the ingenious combination of nano-sized superparamagnetic beads and a strong magnetic field in our MACS Columns. Only this technology ensures minimal labeling of target cells and the preservation of cellular properties. Cell separation with MACS MicroBeads is based on three easy steps: magnetic labeling, magnetic separation, and elution of labeled cells (fig. 1).

For more information on MACS MicroBeads please visit miltenyibiotec.com/microbeads

Figure 1: It only takes three easy steps to get viable cells with high yield and purity from your sample.

Watch how to isolate cells in three easy steps at miltenyibiotec.com/3-easy-steps
MACS® Columns – maximal magnetic power for minimal cell labeling

At the heart of MACS® MicroBead Technology is the MACS Column, containing a matrix composed of ferromagnetic spheres covered with a cell-friendly coating.

When the column is placed in a MACS Separator, the spheres amplify the magnetic field by 10,000-fold, thus inducing a strong magnetic force within the column. The magnetic field efficiently retains cells labeled with the small, nano-sized beads.

The spacious matrix inside the MACS Columns ensures that unlabeled cells can easily flow through while minimally labeled cells (fig. 4) are gently yet effectively retained (fig. 5). This minimizes stress on the cells and allows for efficient washing while preventing cell aggregation.

MACS® Columns enable gentle flow of cells. No pressure, sticking, or compression.

Figure 2: MACS Columns were developed for the fast separation of any cell type labeled with MACS MicroBeads.

Figure 3: MACS Column placed in a MidiMACS™ Separator.

Tailored formats for excellent results – find the optimal column for your cells at miltenyibiotec.com/columns

LEARN MORE

Figure 4: Without the use of a MACS Column, extensive labeling or large beads are needed for an adequate magnetic retention. Only when using MACS Columns, the amplification of the magnetic force ensures effective cell retention with minimal labeling using the small beads.

MACS® Columns enable gentle flow of cells. No pressure, sticking, or compression.

Figure 5: The MACS Column at a glance. Cells move freely between the spheres inside the column and are only retained by magnetic forces.

Column matrix
- Designed and manufactured to deliver maximum purity and yield of viable cells
- The space between the spheres is about 20 times the size of lymphocytes
- Gentle to cells as they can freely flow through
The MACS® Technology advantage

Select the best by combining MACS® Columns and MicroBeads

<table>
<thead>
<tr>
<th>Advantage of column-based technology</th>
<th>Disadvantages of column-free technology</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="MACS MicroBead Technology" /></td>
<td><img src="image" alt="Competing column-free technology" /></td>
</tr>
<tr>
<td>Strong magnetic force</td>
<td>Weak magnetic force</td>
</tr>
<tr>
<td>Minimal labeling suffices</td>
<td>Massive labeling required</td>
</tr>
<tr>
<td><img src="image" alt="Benefits of minimal labeling" /></td>
<td><img src="image" alt="Consequences of massive labeling" /></td>
</tr>
<tr>
<td>• No non-specific labeling</td>
<td>• Non-specific labeling</td>
</tr>
<tr>
<td>• No cell activation</td>
<td>• Cell activation</td>
</tr>
<tr>
<td>• No alteration of cell characteristics</td>
<td>• Alteration of cell characteristics</td>
</tr>
</tbody>
</table>

Why you select the best with MACS Technology:

- Effective separation: maximum purity and recovery
- Small bead size and minimal labeling: preserved cell functionality
- No cell stress: highest cell viability
- Free epitopes, no bead aggregation, no epitope cross-linking: full downstream compatibility

Figure 6: Human PBMCs were either labeled with MACS CD3 MicroBeads for the isolation of T cells with a MACS Column or with other nano-sized beads for column-free isolation of the same cell type. Scanning electron microscopy showed (A) no visible labeling on the cell surface after isolation with MACS MicroBeads and MACS Columns, whereas (B) excessive labeling became obvious (indicated by arrows) after isolation with column-free technology from another manufacturer.

Figure 7: Light microscopic analysis of human PBMC cultures labeled with MACS CD3 MicroBeads or with nano-sized beads from another manufacturer. (A) No bead accumulation in cell culture observed with MACS MicroBeads. (B) Clearly visible bead aggregation (brown) with the other technology.
Cell isolation from single-cell suspensions and dissociated tissues

MACS® MicroBeads and MicroBead Kits

Straightforward positive selection of target cells based on specific markers

The strong magnetic field generated by the matrix in the MACS® Column allows for minimal labeling of target cells with nano-sized MicroBeads. This ensures that plenty of surface epitopes remain free for subsequent fluorescent staining and flow cytometry analysis. Moreover, low labeling concentrations and the small size of MACS MicroBeads do not lead to activation of target cells (fig. 8).

- The least manipulative positive selection method
- Preservation of cell functionality due to optimal labeling
- Biodegradable: labeled cells are ready for downstream applications

MACS® Cell Isolation Kits

Depletion of non-target cells to obtain pure, truly untouched cells

MACS® Cell Isolation Kits contain a cocktail of titrated antibodies and MACS MicroBeads for indirect magnetic labeling (fig. 9). They are the preferred choice if binding of antibodies to the target cells is not desired. Minimal labeling of unwanted cells with MACS MicroBeads avoids non-specific labeling of target cells, leaving the target cells truly untouched (fig. 10). In contrast, column-free methods based on nano-sized beads from other manufacturers require high concentrations of labeling reagents resulting in non-specific labeling of the target cell fraction.

- High purity and recovery rates
- Fully compatible with any downstream application
- No non-specific labeling of target cells

**Figure 8:** Human B cells were enriched using MACS CD19 MicroBeads or a column-free positive selection method from another manufacturer. Subsequently, cells were cultured for 7 days in the presence or absence of the B cell stimulation reagents CD40-Ligand/Anti-His antibody and IL-4. Activation markers (CD69, CD80, and CD86) were measured by flow cytometry directly after cell isolation and after cultivation with and without stimulation. MACS MicroBeads did not alter the status of the target cells, whereas the column-free method led to the activation of B cells in the absence of stimulation reagents.

**Figure 9:** Non-target cells are magnetically labeled and depleted. During separation, the unlabeled target cell type is collected in the flow-through fraction. The labeled non-target cells are retained within the column.

**Figure 10:** Monocytes were enriched by depletion of unwanted cells using (A) the MACS Monocyte Isolation Kit II, human or (B) a column-free kit for human monocyte isolation from another manufacturer. Staining of monocytes (red) and nano-sized beads (green) after isolation showed non-specific labeling of the target cells when using column-free kits, while MACS Technology provided truly untouched cells.

\[
\begin{array}{c|c|c|c}
\text{Percentage of cells showing expression of measured activation markers} & \text{Before separation} & \text{MACS Technology} & \text{Column-free method} \\
\hline
\text{CD69} & * & ** & *** \\
\text{CD80} & * & ** & *** \\
\text{CD86} & * & ** & *** \\
\end{array}
\]

* Directly after separation, **Stimulated 7 days, ***Unstimulated 7 days
Cell isolation directly from blood products

StraightFrom® Technology

**Cell isolation directly from blood products without density gradient centrifugation**

StraightFrom® MicroBeads allow magnetic isolation of various leukocyte subsets from different starting materials by positive selection. With these kits, isolation of leukocyte subsets has never been easier and quicker. In contrast to conventional methods, StraightFrom Technology does not require density gradient centrifugation (fig. 11).

- Start directly with whole blood, buffy coat, and leukocyte reduction system chamber (LRSC)
- The isolated target cells are immediately ready for any downstream application
- Simple protocol with only a few handling steps

<table>
<thead>
<tr>
<th>StraightFrom MicroBeads protocol</th>
<th>Conventional protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfer and dilute sample</td>
<td>Transfer and dilute sample</td>
</tr>
<tr>
<td>Magnetic labeling</td>
<td>Layer density gradient medium</td>
</tr>
<tr>
<td>Cell separation</td>
<td>Density gradient centrifugation without brake</td>
</tr>
<tr>
<td><strong>&lt;30 min</strong></td>
<td>PBMC separation and wash</td>
</tr>
<tr>
<td></td>
<td>Cell count</td>
</tr>
<tr>
<td></td>
<td>Magnetic labeling</td>
</tr>
<tr>
<td></td>
<td>Cell separation</td>
</tr>
<tr>
<td></td>
<td><strong>&gt;2 h</strong></td>
</tr>
</tbody>
</table>

**MACSxpress® Technology**

**With high speed to untouched target cells**

MACSxpress® Technology enables the fastest large-scale isolation of untouched cells directly from whole blood – without the need for any centrifugation. Micro-sized MACSxpress Beads allow for minimal labeling to prevent non-specific labeling and activation of target cells. Non-target cells are removed by immunomagnetic depletion. Simultaneously, erythrocytes are sedimented to yield target cells of exceptional purity (fig. 12).

- Go from whole blood to pure cells within 20 minutes
- Obtain untouched target cells directly from whole blood
- No density gradient centrifugation, erythrocyte lysis or cell counting required

Add reconstituted MACSxpress Cell Isolation Cocktail to whole blood.

Place tube in the magnetic field of the MACSxpress Separator for 15 minutes.

Collect the supernatant which contains the unlabeled target cells.

**Total: 20 min**

**Figure 11:** Comparison of the StraightFrom MicroBeads protocol with conventional protocols, demonstrating the simplicity and short hands-on time.

**Figure 12:** MACSxpress Technology allows the isolation of cells from whole blood within 20 minutes.
**The next step in flexibility – label-free cells and challenging samples**

**REAlease™ Technology**

**Get bead- and label-free cells**

REAlease™ MicroBead Kits have been developed for positive selection of target cells from PBMCs. REAlease MicroBead Technology relies on recombinantly engineered antibody fragments instead of antibodies to label specific cell surface markers. The antibody fragments have a low affinity for cell surface epitopes. However, when the fragments are multimerized as a complex, they bind epitopes with high avidity and enable effective magnetic cell separation. REAlease Technology controls the multimer/monomer state of the fragments and thus triggers the release of monomerized antibody fragments from the cell surface after isolation. Ultimately, the isolated cells are free from antibody fragments and magnetic labels.

- Bead-free cells: suited for second round of magnetic labeling
- Label-free cells: the epitope of a marker becomes completely available again
- Recombinantly produced: lot-to-lot consistency allows for reproducible results

**UltraPure MicroBeads**

**Minimize debris for high-quality results**

UltraPure MicroBeads have been particularly optimized for use with challenging samples. The unique formulation provides compelling benefits particularly when starting with materials that contain large amounts of cell debris or low numbers of target cells. UltraPure MicroBeads greatly improve recovery and purity of the sorted population by specifically enriching viable target cells (fig. 13).

- Optimized formulation to minimize debris
- High cell purity, even from challenging starting materials
- As easy to use as the classic MACS® MicroBeads

**Figure 13:** CD34+ cells were isolated with the column-based CD34 MicroBead Kit UltraPure (upper plots) or with a column-free positive selection method from another manufacturer (lower plots). The cell population purified with MACS MicroBeads UltraPure showed greatly reduced amounts of debris compared to the column-free method.

Find the separation strategy that best fits your needs at [miltenyibiotec.com/separation-strategies](miltenyibiotec.com/separation-strategies)

Learn more about REAlease MicroBead Technology at [miltenyibiotec.com/realease-microbeads](miltenyibiotec.com/realease-microbeads)
From manual to fully automated high-throughput cell isolation

**Manual separation**

Ease-of-use with manual MACS® Separators for simple and straightforward setups in any lab.

- The ideal solution for low-throughput experiments
- Proven technology in over 30,000 publications
- Perfectly tailored solutions for your experimental needs

![Figure 14: Manual MACS Separators equipped with MACS Columns.](image)

**autoMACS® Pro Separator**

Fully automated benchtop instrument for magnetic cell separation of multiple samples.

- Walk-away automation with cell labeling and isolation of up to six samples
- Standardized cell separation for reproducible, user-independent results
- Intuitive, easy-to-use software interface for a multi-user environment

![Figure 15: Fully automated labeling and separation for the most convenient way to obtain pure cell populations with the autoMACS Pro Separator.](image)

Miltenyi Biotec offers comprehensive technical support for both new and advanced users alike. Our experienced technical support teams have the knowledge and expertise to answer your questions.

You can reach us at your convenience by e-mail, phone, or online in our forums and Live Chat – find all the information at [miltenyibiotech.com/support](miltenyibiotech.com/support)

No question is too big or small.
MultiMACS™ Cell24 Separator Plus

Efficient, semi-automatic cell isolation of large sample volumes or numbers.

- Convenient and easy handling of up to 24 samples in parallel or large sample volumes
- Compatible with any starting material and cell separation strategy
- Reliable, standardized process for reproducible results

MultiMACS™ X

Walk-away solution for high-throughput setups – the next level of automated cell separation.

- The benefits of the MultiMACS™ Cell24 Separator Plus integrated into a liquid handler for minimal hands-on time
- Tailored solutions for your specific application
- Sample tracking, run reports, and LIMS integration

Figure 16: Functional design for the isolation of large sample numbers or volumes with the semi-automated MultiMACS Cell24 Separator Plus.

Simultaneous multisample magnetic cell separation with the MultiMACS™ Cell24 Separator Plus

LEARN MORE

miltenyibiotec.com/multimacs

Figure 17: Full automation, high-throughput processing, and sample tracking for true walk-away cell isolation with the MultiMACS X.

MultiMACS X – designed to speed up automated cell separation

LEARN MORE

miltenyibiotec.com/multimacsx
Miltenyi Biotec provides products and services worldwide. Visit www.miltenyibiotech.com/local to find your nearest Miltenyi Biotec contact.

Unless otherwise specifically indicated, Miltenyi Biotec products and services are for research use only and not for therapeutic or diagnostic use. autoMACS, MACS, the MACS logo, MACSxpress, MidiMACS, MultiMACS, REAlease, and StraightFrom are registered trademarks or trademarks of Miltenyi Biotec GmbH and/or its affiliates in various countries worldwide. Copyright © 2017 Miltenyi Biotec GmbH and/or its affiliates. All rights reserved.