

# MACS® Sample Preparation Start smart with innovative solutions for your samples



### **Start smart**

The success of your experiment starts at the very beginning. Our smart solutions for sample preparation support you with optimized protocols for the dissociation of virtually any tissue.

Get viable single-cell suspensions or homogenous tissue lysates for your downstream application and standardize your laboratory workflow right from the start.

# Keep it fresh – store tissue and keep its primary state

The MACS® Tissue Storage Solution allows optimized storage of fresh organ and tissue samples for at least 48 hours without activating cells or inducing apoptosis.

# Be gentle – get viable cells with preserved epitopes

gentleMACS™ Technology delivers viable cells from solid tissues in a fast, standardized, and user-independent way, which preserves cellular composition and surface epitopes.

# Clean it – remove cell aggregates and other unwanted material

Innovative cell strainers and cleaning reagents help you to tune your sample for your downstream application by the removal of cell aggregates, debris, or other unwanted material, such as myelin, dead cells, or erythrocytes.



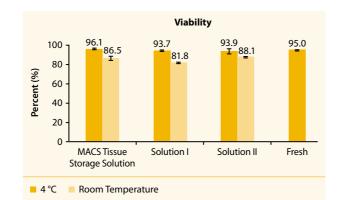


## **Convenient tissue storage**

The MACS® Tissue Storage Solution allows for optimized storage of fresh organ and tissue samples to gain flexibility and to preserve the primary state for at least 48 hours. It has been tested and is compatible with variety of human and rodent tissues including tumor, skin, heart, spleen, brain, and skeletal muscle.

### Gain flexibility

The MACS Tissue Storage Solution has been developed to avoid background effects, like cell activation or apoptosis induction that may occur in storage. Store your samples for 48 hours at 4 °C and process them at your convenience.



**Figure 1:** Comparison between MACS Tissue Storage Solution and two GMP-grade organ transplant solutions from other manufacturers.

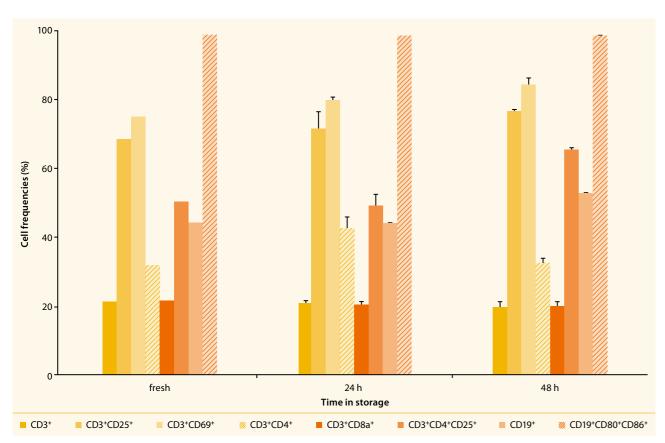


Figure 2: Tumor tissue stored for 24 h or 48 h at 4°C in MACS Tissue Storage Solution. After dissociation, TIL populations from obtained cell suspensions were analyzed by flow cytometry.





## gentleMACS™ Technology

# Developed for the most reliable results

gentleMACS Technology allows fully automated tissue dissociation in a closed and sterile system to generate tissue lysates or viable single-cell suspensions with high viability and preserved surface epitopes.

With the unique combination of alternating incubation time of enzymatic digestion and mechanical disruption, enzyme activity and shearing forces are lowered to a minimum. This makes gentleMACS Technology the most gentle and convenient method for standardized and reproducible tissue dissociation.

### Enzymatic treatment

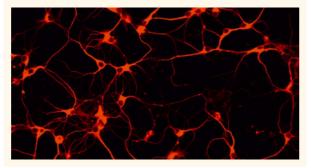
Tissue-specific enzymes soften the tissue by degrading the extracellular matrix and adhesion molecules.

#### Mechanical disruption

Low mechanical shearing constantly disrupts the tissue, exposing it to the enzymes.







**Figure 3:** Adult rodent neurons dissociated with the Neuron Isolation Kit and stained with ß III Tubulin antibody.

## gentleMACS™ Dissociators

### Automated tissue dissociation on your bench

# gentleMACS Dissociator and gentleMACS Octo Dissociator

The gentleMACS and gentleMACS Octo Dissociators offer reliable tissue dissociation and thorough homogenization with pre-defined programs and parallel sample processing. The gentleMACS can process two samples in parallel with over 40 pre-defined programs. The gentleMACS Octo can process eight samples in parallel or independently and allows for the creation of user-defined programs.

### MACSmix™ Tube Rotator

The MACSmix Tube Rotator is a helpful tool for the enzymatic digestion steps during tissue dissociation with a gentleMACS Dissociator. It is a versatile instrument powered by rechargeable batteries operating independently of a permanent power supply. It is suitable for a temperature range of 2 °C to 42 °C and can be placed in a refrigerator or incubator.

# gentleMACS Octo Dissociator with Heaters

The gentleMACS Octo Dissociator with Heaters extends the basic features of the gentleMACS Octo Dissociator for maximum convenience, flexibility, and efficiency.

#### Full automation with integrated heaters

The heaters enable enzyme incubation directly on the instrument for walk-away tissue dissociation with enzymatic digestion.

### **High-throughput processing for faster results**

The gentleMACS Octo Dissociator with Heaters can process up to eight samples either in parallel or independently.

### **Independent sample operation**

Different tissue types can be processed simultaneously. Add samples at any time, even if other dissociation programs are in progress.

### **Customize your dissociation program**

In addition to over 40 pre-defined programs, you can create your own programs for your specific samples and applications to dissociate virtually any tissue type



### gentleMACS™ Tubes

The gentleMACS Tube is a central component of gentleMACS Technology. Each element of the tube has been engineered to ensure the highest performance in the dissociation or homogenization of your tissue samples. The cap has a rotor-stator-system to apply gentle mechanical shearing to tissue.

VIDEO



Choose the right tube for your experiments with the help of this fun video:

miltenyibiotec.com/ gentlemacstubes/p10 Dedicated tubes for specific applications:

- Tissue dissociation: Use the purple-cap
   C Tube for gentle tissue disruption to get viable single-cell suspensions for cell separation, cell culture, and cell analysis experiments.
- Tissue homogenization: Choose the orange-cap M Tube to achieve thorough sample homogenization for subsequent molecular and microbiology analysis.



### Tube enclosure – functional design

Our patented enclosure design directs the sample flow towards the stator to ensure thorough dissociation and homogenization.

### Spacers – make the difference

The stator teeth of C Tubes are equipped with spacers that define a specific distance between the rotor and the stator. This ensures efficient extraction of viable single cells from tissues.

M Tubes lack spacers, enabling them to perform tissue homogenization for applications in molecular and microbiology.

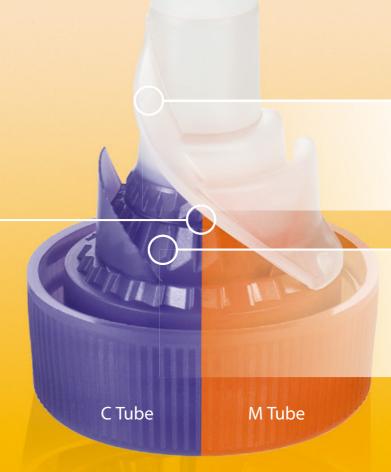


### Rotor – crafted precision

A rotating paddle draws the sample into the stator for processing. It provides the exact amount of shear force necessary to extract intact cells or molecules from tissues.

### Stator – exact control

At the fixed stator site, the sample is processed through mechanical shearing. M Tubes lyse the cells by grinding the tissue. Within C Tubes, a defined gap between the rotor and stator keeps cells intact, producing viable single-cell suspensions.



### **MACS® Tissue Dissociation Kits**

MACS Tissue Dissociation Kits offer a broad variety of ready-to-use kits, which allow for gentle and effective dissociation of human and rodent tissues.

### Tissue specific enzyme composition

The convenient tissue-specific kit format provides pre-defined enzyme solutions compiled and titrated to match individual tissue needs for optimal results.

### Lot-to-lot consistency

Efficacy and epitope sensitivity tests are part of our routine enzyme quality control to provide consistent performance and reproducibility for your experiments.

### **Epitope preservation**

Highly purified enzymes with specific activities keep cellular surface markers intact while effectively degrading extracellular matrices and adhesion molecules during tissue dissociation. We have put together epitope preservation lists which consist of over 200 epitopes that have been tested for sensitivity after enzymatic digestion with our Tumor Dissociation Kits or Multi Tissue Dissociation Kits.





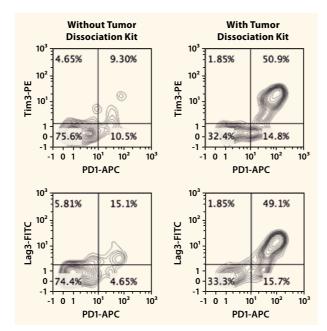


Figure 4: Efficient recovery of CD8<sup>+</sup> TILs from B16-F10 tumors with the Tumor Tissue Dissociation Kit. B16-F10 mouse tumors were collected and dissociated using the gentleMACS Octo Dissociator with Heaters in the presence or absence of the Tumor Dissociation Kit, mouse enzymes. Cells were subsequently labeled with REAfinity™ Antibodies and analyzed using a MACSQuant® Analyzer.

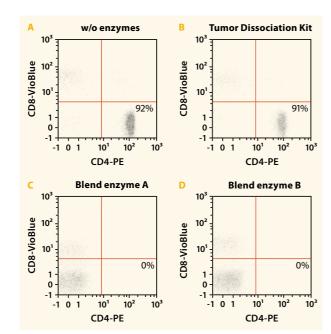


Figure 5: Comparison of epitope preservation after incubation of peripheral mononuclear cells (PBMC) with the respective enzymes. (A) Control: no enzymes added, (B) Enzyme cocktail of the Tumor Dissociation Kit, human from Miltenyi Biotec, (C) Alternative blend enzyme A, (D) Alternative blend enzyme B.

### Tissue-specific enzyme kits

For optimal dissociation of different tissues into single-cell suspensions we have developed 20 different tissue-specific enzyme kits to be used in combination with over 40 gentleMACS™ Programs. Many programs and kits have been optimized to obtain high yields of specific cell populations, including rodent neurons, neonatal rodent cardiomyocytes, tumor cells, immune cells, and stem cells.

Our Multi Tissue Dissociation Kits have been developed for the gentle and effective isolation of different cell types from various tissues, such as kidney, prostate, mouse embryo, and cell monolayers.

### Mouse tissues

- Tumor
- Neonatal brain (<P7)</li>
- Adult brain (>P7)
- Neurospheres
- Lamina propria (Colon)
- LungSpleen
- Prostate
- Embryoid bodies

### Human tissues

- Tumor
- Whole skin
- Epidermis
- Umbilical cord

Neonatal heart

· Skeletal muscle

Adipose tissue

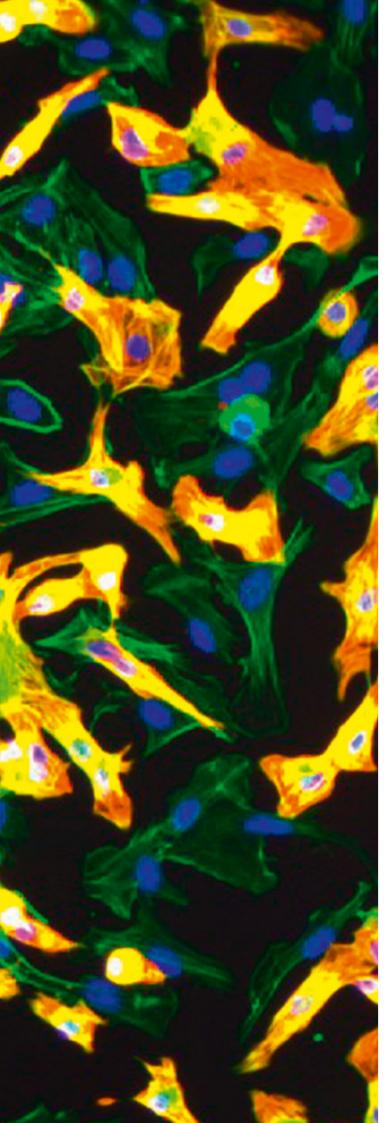
Epidermis

Liver

- Embryoid bodies
- is Kidney



According to customers' publications, certain kits for mouse tissues also work for human tissues. Contact our technical support team to find out more about which kit is right for your tissue.



# Efficient sample cleaning

Cell suspensions are often complex and unwanted material, like dead cells, debris, and red blood cells, can have interfering effects on downstream applications. Our cell strainers and removal reagents effectively clean and prepare your sample for downstream assays.

### Smart strainers and filters

MACS® SmartStrainers can be used for the removal of larger particles from cell suspensions of dissociated tissue or blood samples:

- Improved ventilation during filtration avoids clogging of the strainers
- Easily fit onto standard 15 mL and 50 mL conical tubes
- Various mesh sizes are available, including 30, 70, and 100 µm to fit your specific application

Pre-Separation Filters are designed for effective and easy removal of cell aggregates from single-cell suspensions after labeling with MACS MicroBeads or antibodies. Using the filters ensures optimal flow within cell separation columns and in flow cytometers.

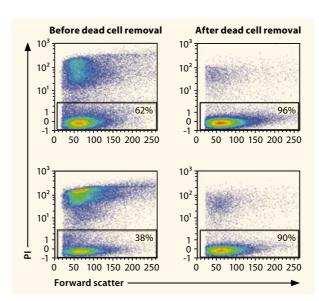
# Dedicated solutions to reduce complexity

Our sample cleaning reagent portfolio provides options to reduce complexity of cell suspensions. Improve the efficiency of antibody binding, isolation of target cells, cell culture conditions, and the quality of genomic analysis by removing unwanted material, such as:

- dead cells
- debris
- endotoxins
- myelin
- · red blood cells

# Effective removal of dead cells and debris

The removal of dead cells improves cell cultivation, reduces flow sorting time, and increases the recovery rate when performing single-cell analysis. Use the Dead Cell Removal Kit for effective magnetic depletion of dead and dying cells when working with robust cells, such as epithelial cells, tumor cells, and immune cells.



**Figure 6:** PBMCs were subjected to heat shock induced cell death for two different time spans – upper panel short time span, lower panel long time span. Subsequently, dead cells were removed using the Dead Cell Removal Kit according to the manufacturer's data sheet. For flow analysis, dead cells were stained using propidium iodide.

The Debris Removal Solution is a ready-to-use density gradient reagent. It allows for the fast removal of debris in cell suspensions containing fragile cells from brain, heart, liver, and kidney, while applying full acceleration and full brake during centrifugation.

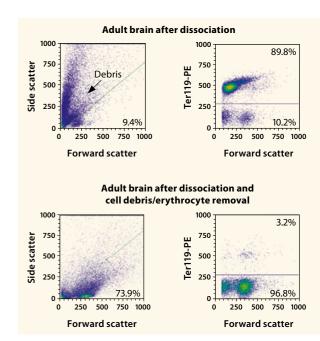


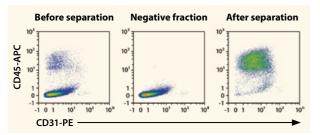
Figure 7: Adult mouse brain was dissociated using the Adult Brain Dissociation Kit, mouse in combination with the gentleMACS Octo Dissociator with Heaters. Subsequently, red blood cells were depleted using the Red Blood Cell Lysis Solution, before removing debris using the Debris Removal Solution. Red blood cells were stained with anti-Ter119-PE. Cells were analyzed by flow cytometry using the MACSQuant Analyzer based on scatter signals to demonstrate absence of debris after



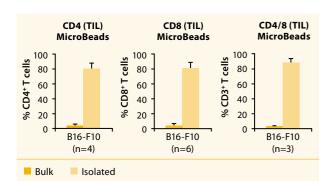
### **Applications**

# TIL isolation and analysis of rare subpopulations from solid tumors

Automated tumor dissociation, using our Tumor Cell Dissociation Kits, is optimized for the efficient recovery of immune cells and tumor cells without impairing the composition of cell surface epitopes. Tumor infiltrating leukocytes (TILs) can be efficiently isolated after human and mouse tumor dissociation using CD45, CD4, CD8, or CD4/CD8 TIL-specific MicroBeads. Enrichment of TILs significantly reduces the time for flow analysis and flow sorting and increases the sensitivity in downstream applications, including single-cell immune profiling.



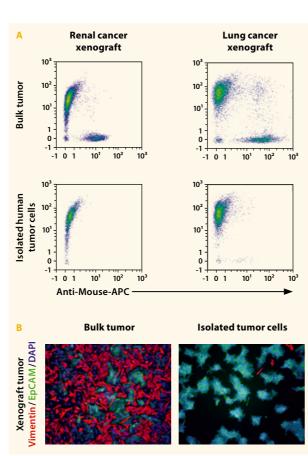
**Figure 8:** Isolation of TILs from mouse solid cancer tissue using CD45 (TIL) MicroBeads, mouse.



**Figure 9:** Isolation of CD4\*, CD8\*, and pan T cells from mouse B16-F10 tumor models using mouse CD4 (TIL) MicroBeads, CD8 (TIL) MicroBeads, and CD4/CD8 (TIL) MicroBeads. Magnetic cell isolation resulted in purities above 80%, which represents an up to 500-fold enrichment of the target cell population.

# Tumor cell isolation for reliable downstream applications

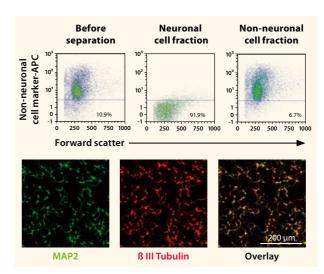
We have developed our MicroBead-based Tumor Isolation Kits and the Mouse Cell Depletion Kit for the fast and easy removal of all non-tumor cells from human, mouse, and PDX tumors. A prerequisite for optimal results is the preservation of cell surface epitopes during the dissociation of the tumors. This can be achieved using the gentleMACS™ Octo Dissociator with Heaters and the Tumor Dissociation Kits for the dissociation of any tumor entity. The subsequent tumor cell isolation allows for the removal of > 95% of contaminating non-tumor cells. Pure tumor cell suspensions significantly increase the quality of downstream applications, especially cell culture and molecular applications.



**Figure 10:** (A) Xenograft tumors were dissociated using the gentleMACS Octo Dissociator with Heaters and the Tumor Dissociation Kit, human according to the datasheet. Non-tumor cells were depleted from the cell suspension using the Mouse Cell Depletion Kit. (B) Upon magnetic separation, the original bulk and isolated tumor cell fractions were cultured for seven days, fixed, and stained. Human tumors were stained for the human-specific epithelial tumor marker CD326 (EpCAM). Even after seven days, the cultures of isolated tumor cells were nearly pure.

# Isolation of viable primary neurons from adult mouse brain

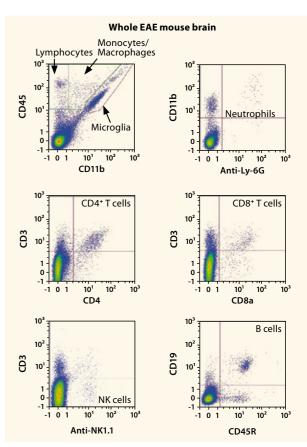
The Adult Brain Dissociation Kit, mouse and rat has been developed for fast and standardized dissociation of adult mouse brain (> P7), yielding viable neural cells, including neurons, astrocytes, oligodendrocytes, and microglia. The included debris removal step enables efficient isolation of specific cell populations. For the isolation of neurons, all non-neurons are removed from the sample, thus allowing for pure neuron cell cultures and targeted functional and molecular analysis.



**Figure 11:** Adult neurons were enriched to over 90% purity from dissociated mouse brain using the Neuron Isolation Kit. After 7 days in cell culture using MACS Neuro Medium supplemented with MACS NeuroBrew®-21 neurons grew to a network as indicated by MAP2 (green) and ß III Tubulin (red staining).

# Analysis of immune cells from inflamed mouse brain and spinal cord

We have developed a dissociation protocol using the gentleMACS™ Octo Dissociator with Heaters and the Multi Tissue Dissociation Kit 1 that ensures the preservation of immune cell-specific epitopes and enables reliable immune cell analysis by flow cytometry.



**Figure 12:** Flow cytometry analysis of immune cell subpopulations from brain from EAE mice. Representative flow cytometric data for the identification of immune cell subpopulations after dissociation of brain (n = 2) from EAE mice using of the Multi Tissue Dissociation Kit 1. Debris, dead cells, and doublets were excluded from the analysis based on scatter signals and propidium iodide fluorescence.



## **Applications**

### Isolation and analysis of tissue-derived mouse dendritic cells

Using the gentleMACS™ Octo Dissociator with Heaters in combination with our Tissue Dissociation Kits for the dissociation of organs and tissues of the immune system yields single-cell suspensions. These include CD11c+ cells with high viability and preserved surface epitopes for subsequent cell isolation and staining. CD11c MicroBeads UltraPure have been optimized for the rapid and simple isolation of mouse DCs from single-cell suspensions generated from lymphoid and non-lymphoid tissues.

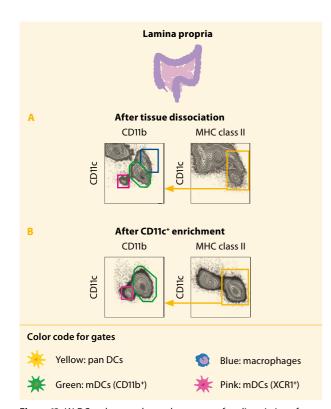


Figure 13: (A) DC and macrophage phenotypes after dissociation of mouse small intestines with the gentleMACS Octo Dissociator with Heaters and the Lamina Propria Dissociation Kit, mouse. Dissociated cells were stained with the specified antibodies and analyzed by flow cytometry. (B) Enrichment of pan DCs and CD11c+ macrophage populations with CD11c MicroBeads Ultrapure. Enriched cells were stained with the specified antibodies and analyzed by flow cytometry.

### Isolation of viable and functional ILC2 from different tissues

Innate lymphoid cells (ILCs) represent an expanding family of innate effector cells that have crucial roles in the generation and maintenance of immunity, especially at mucosal surfaces.

The gentleMACS Octo Dissociator with Heaters and MACS® Tissue Dissociation Kits provide the opportunity to standardize the procedure to obtain ILC2 from different tissue sources and generate reproducible results.

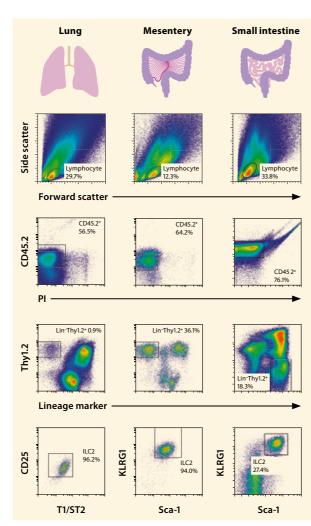


Figure 14: ILC2 after dissociation of mouse lung, mesentery, and small intestine with the gentleMACS Octo Dissociator with Heaters and respective MACS Tissue Dissociation Kits. Dissociated cells were stained with the specified antibodies and analyzed by flow cytometry. For detailed information on the gating strategy, please refer to the respective application note.

gentleMACS™ Dissociators and Tubes gentleMACS Dissociator	
gentle MACS Dissociator	
	130-093-235
gentleMACS Octo Dissociator	130-095-937
gentleMACS Octo Dissociator with Heaters	130-096-427
MACSmix Tube Rotator	130-090-753
C Tubes – 25 tubes*	130-093-237
C Tubes – 100 tubes**	130-096-334
M Tubes – 25 tubes*	130-093-236
M Tubes – 100 tubes**	130-096-335
M Tubes with Strainer, 50 tubes	130-094-392
Tumor tissue	
Brain Tumor Dissociation Kit (P), human	130-095-942
FFPE Tissue Dissociation Kit	130-118-052
Tumor Dissociation Kit, human	130-095-929
Tumor Dissociation Kit, mouse	130-096-730
Neural tissue	
Adult Brain Dissociation Kit	130-107-677
Neural Tissue Dissociation Kit (P)	130-092-628
Neural Tissue Dissociation Kit (T)	130-093-231
Neural Tissue Dissociation Kit – Postnatal Neurons	130-094-802
Neurosphere Dissociation Kit (P)	130-095-943
Immune tissue	
Epidermis Dissociation Kit, human	130-103-464
Epidermis Dissociation Kit, mouse	130-095-928
Lamina Propria Dissociation Kit, mouse	130-097-410
Liver Dissociation Kit, mouse	130-105-807
Lung Dissociation Kit, mouse	130-095-927
Spleen Dissociation Kit, mouse	130-095-926
Whole Skin Dissociation Kit, human	130-101-540

Product	Order no.
Other tissues	
Adipose Tissue Dissociation Kit, mouse, rat	130-105-808
Embryoid Body Dissociation Kit, human and mouse	130-096-348
Neonatal Heart Dissociation Kit, mouse, rat	130-098-373
Skeletal Muscle Dissociation Kit, mouse, rat	130-098-305
Umbilical Cord Dissociation Kit, human	130-105-737
Multi Tissue Dissociation Kit 1	130-110-201
Multi Tissue Dissociation Kit 2	130-110-203
Multi Tissue Dissociation Kit 3	130-110-204
Filters and Strainers	
Pre-Separation Filters (20 μm), 50 filters*	130-101-812
Pre-Separation Filters (30 μm), 50 filters*	130-041-407
Pre-Separation Filters (70 μm), 50 filters*	130-095-823
MACS SmartStrainers (30 μm), 50 filters*	130-098-458
MACS SmartStrainers (70 μm), 50 filters*	130-098-462
MACS SmartStrainers (100 μm), 50 filters*	130-098-463
MACS SmartStrainers (30 μm), 100 filters**	130-110-915
MACS SmartStrainers (70 μm), 100 filters**	130-110-916
MACS SmartStrainers (100 μm), 100 filters**	130-110-917
Removal reagents	
Dead Cell Removal Kit	130-090-101
Annexin V Micro Bead Kit	130-090-201
Endotoxin Removal Beads	130-093-657
MACS Tissue Storage Solution	130-100-008
Red Blood Cell Lysis Solution (10x)	130-094-183
Myelin Removal Beads II, human, mouse, rat	130-096-733
Debris Removal Solution	130-109-398
*sterile, single-packed **sterile, packed as 4×25 pieces	

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