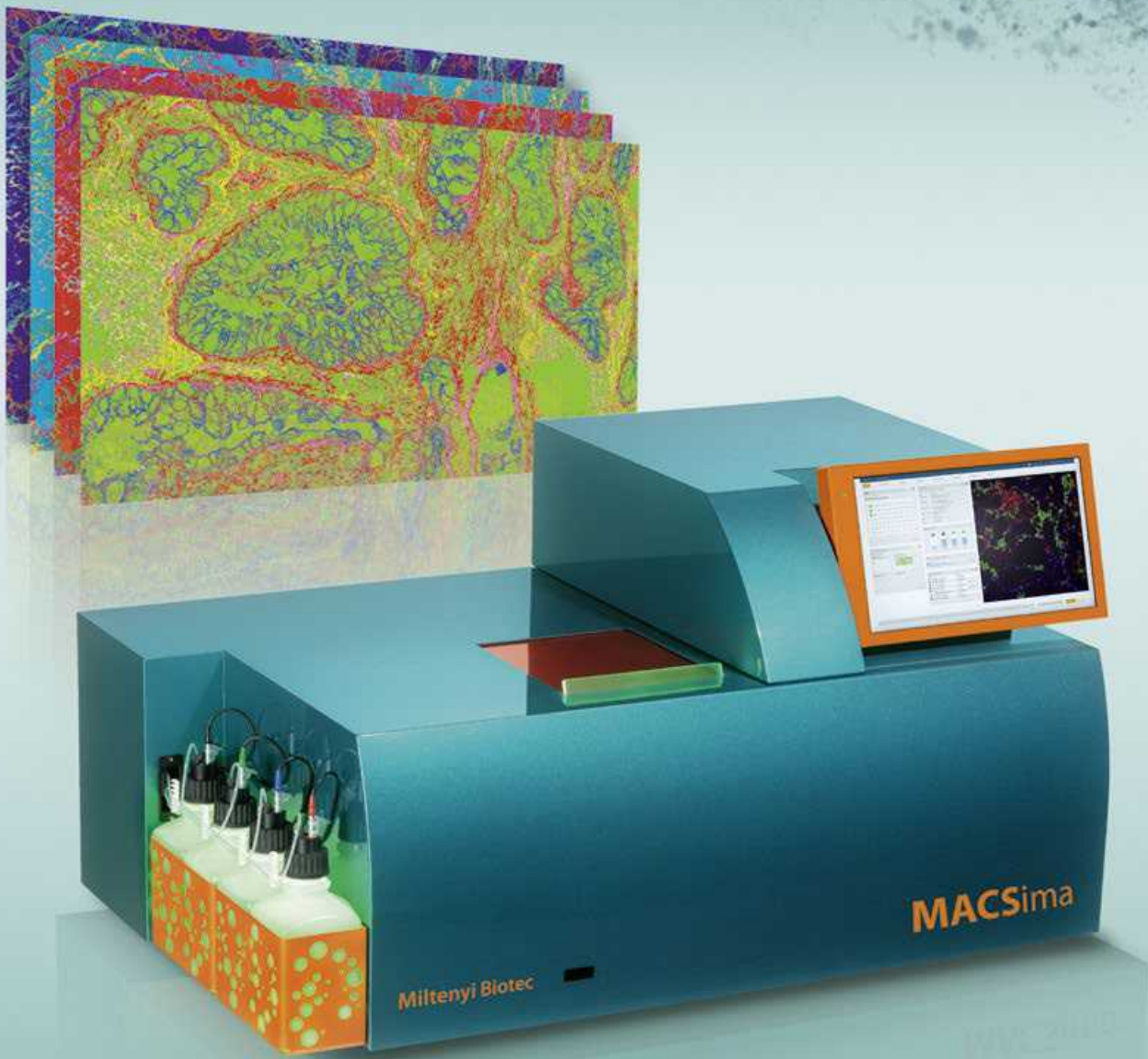




Miltenyi Biotec

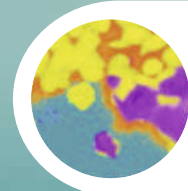
# MACSima™ Platform

Explore the full potential of spatial biology



博克科技股份有限公司

J&H TECHNOLOGY CO., LTD.



UNDERSTAND  
NATURE'S  
COMPLEXITY

# The MACSima™ Platform

## Easily understand the complex interplay of cells in tissues

In our body's tissues, cells interact closely, affecting each other's functions and states. For example, in the tumor microenvironment, cancer cells can stop immune cells from working properly.

Those cellular complexities cannot be fully understood by analyzing individual cells or cell suspensions. We need to study them in their spatial context in their natural settings – the essence of spatial biology.

Enter the world of spatial biology with the high-plex proteomic approach of the MACSima Platform. Benefit from unparalleled flexibility: Analyze hundreds of protein markers across every cell in your tissue sample or focus on a more specific panel of around 20 markers for targeted or preliminary studies. Don't stop at proteins. Go deeper with spatial RNA detection, seamlessly integrated into the MACSima Platform for a unified multiomics workflow and analysis on the same tissue section.

Returning to the example of the tumor microenvironment, this can help us uncover why certain cells fail to do their job or why specific drugs aren't effective.

Content  
without context  
is just noise.

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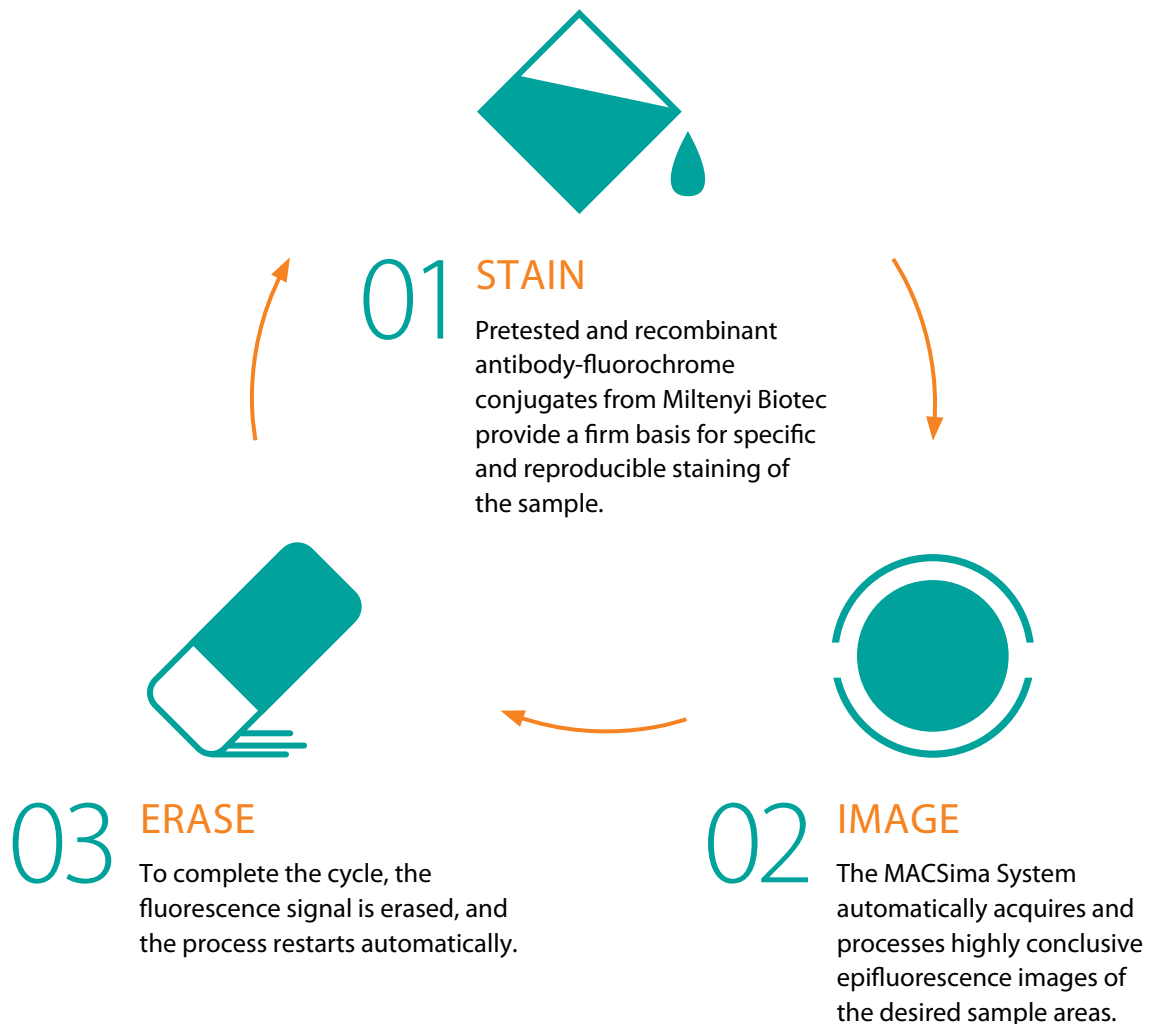
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# MICS technology – the basic principle

The MACSima Platform utilizes MICS (MACSima Imaging Cyclic Staining) technology. This approach captures microscopy data of hundreds of markers without compromising the sample for further downstream processing. MICS involves three steps, all performed by the MACSima System in a fully automated manner. Initially, the sample is stained with multiple fluorochrome-conjugated antibodies.

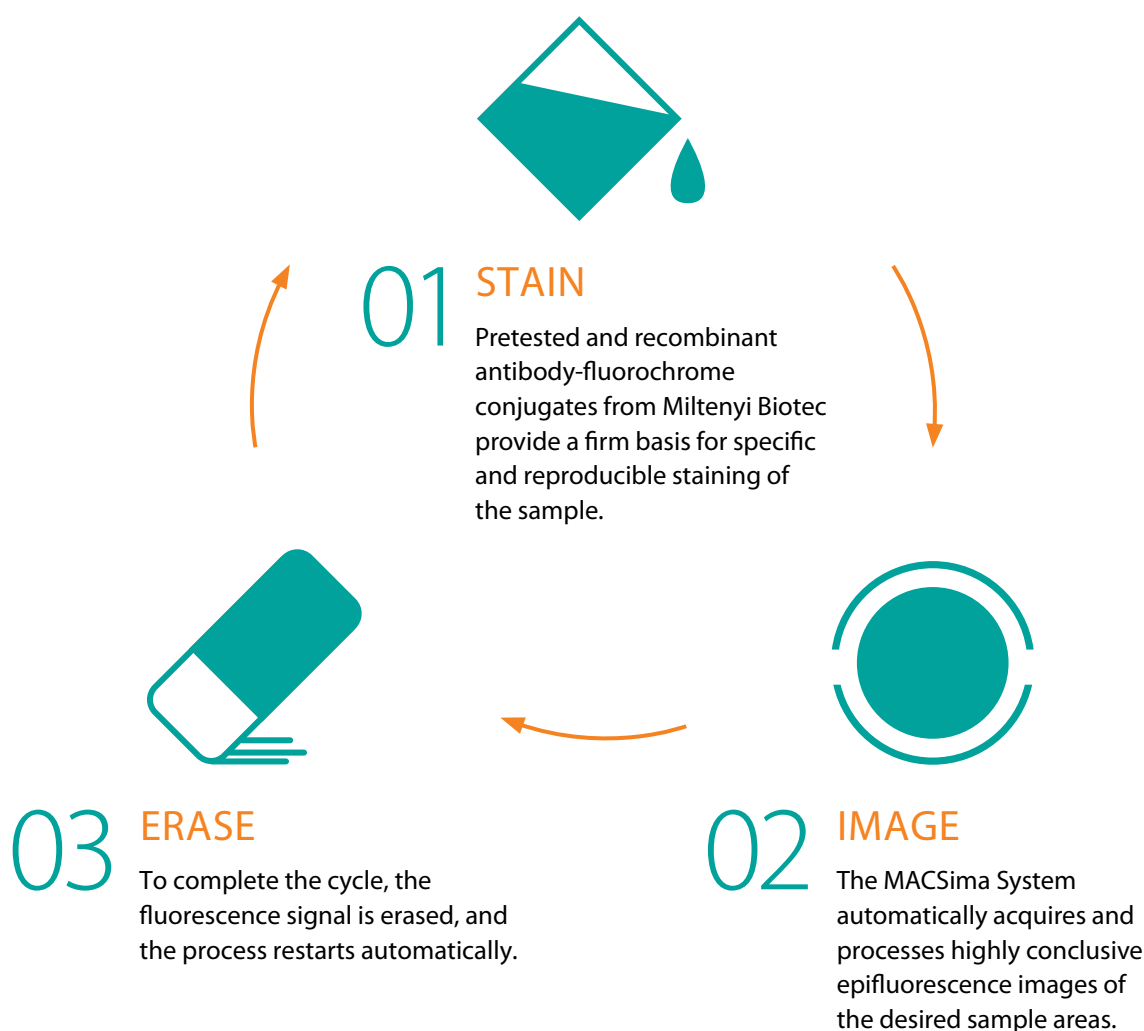
Utilize our pretested antibody portfolio or enjoy the flexibility to employ your own antibodies. In the subsequent step, an image is captured using the widefield microscope, and to conclude the cycle, the fluorescence signal is erased. This cycle is automatically repeated as many times as necessary, enabling the user to label an unlimited number of markers.



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Ready, set, explore!  
Your shortcut to spatial data.



- 1 Panel design**  
Accelerated and simplified preexperimental work with Miltenyi Biotec's pretested recombinant antibodies and plug-and-play antibody panels.



2

### Automated MICS experiment

Efficiency through automation of the MACSima System, saving time for tackling other challenges in your project.



3

### Spatial data analysis

Rapid generation of conclusive and publication-ready results with MACS iQ View – Spatial Biology, an intuitive software that makes complex spatial data analysis accessible to users of all backgrounds.

MACSima

# MACSima System

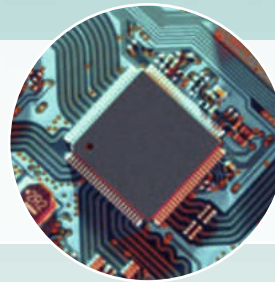
## Fully automated sample handling and data acquisition

Excellent optics, a state-of-the-art sCMOS camera, accurate liquid handling, and high computer capacity are the hallmarks of the MACSima System.

Experience hands-free MICS experiments with our system components that operate in perfect harmony.

### Computers

Two computers with high storage capacity allow for detailed data analysis while the image stack continues to grow cycle after cycle.



### Liquid handling system

The robotic needle arm eliminates pipetting errors and saves valuable time as it can handle hundreds of antibodies and all other necessary liquids accurately and fully automatically. Automated washing processes prevent carryover of reagents to maintain fluorescent signal specificity across all images.



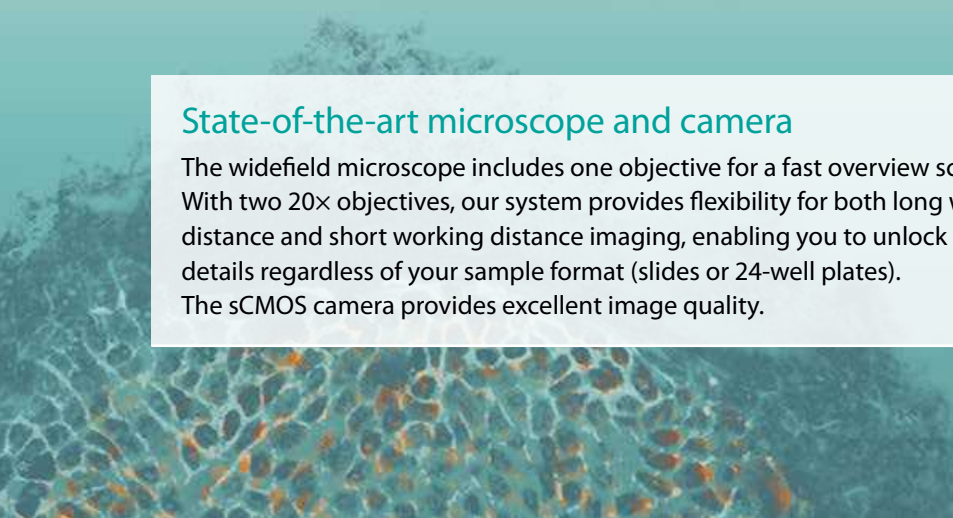
### Ultraprecise stage

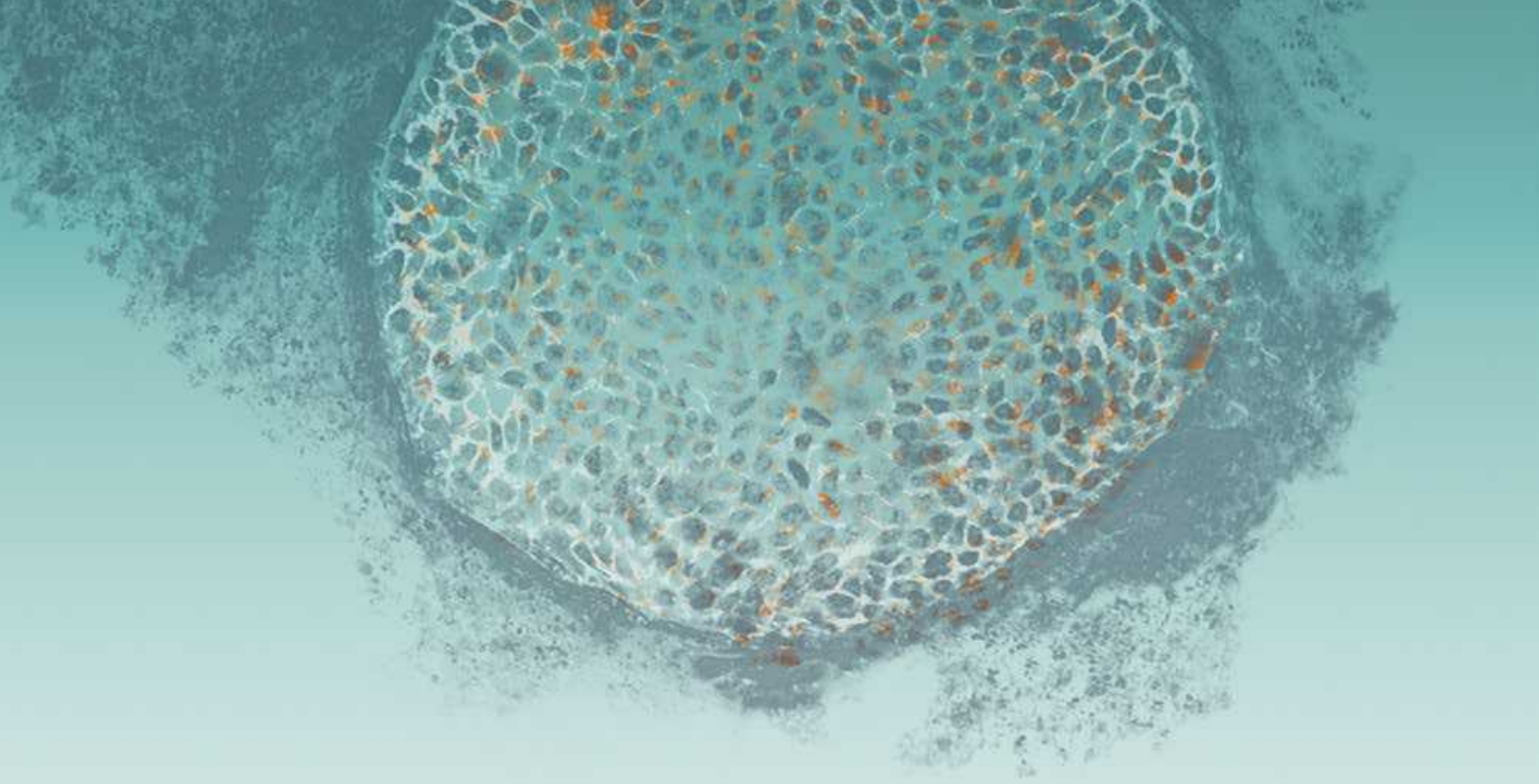
Hosting the sample and all reagents, the ultraprecise stage serves as the MACSima System's work bench. Accurate positioning of all components throughout the MICS experiment ensures reliable execution of the iterative process and exact maintenance of the field of view.



### State-of-the-art microscope and camera

The widefield microscope includes one objective for a fast overview scan. With two 20x objectives, our system provides flexibility for both long working distance and short working distance imaging, enabling you to unlock subcellular details regardless of your sample format (slides or 24-well plates). The sCMOS camera provides excellent image quality.





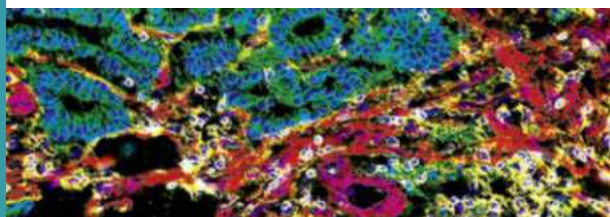
# MACSwell Sample Carriers

## Analyze any kind of fixed sample

To answer complex scientific questions, you shouldn't be held back by technical constraints. That's why we developed MACSwell Sample Carriers for the MACSima System, providing you with total flexibility in analyzing fixed samples.

These carriers are designed to support various types of samples, including tissues, adherent cells, and suspension cells. Each carrier features a precisely designed reaction cavity, ensuring confidence and trouble-free MICS experiments.

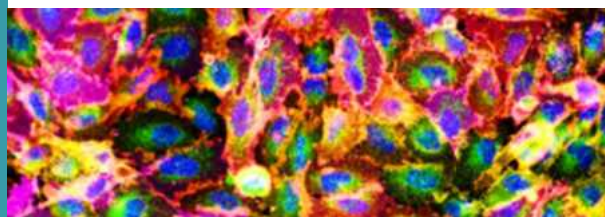
### TISSUE



### MACSwell Imaging Frames

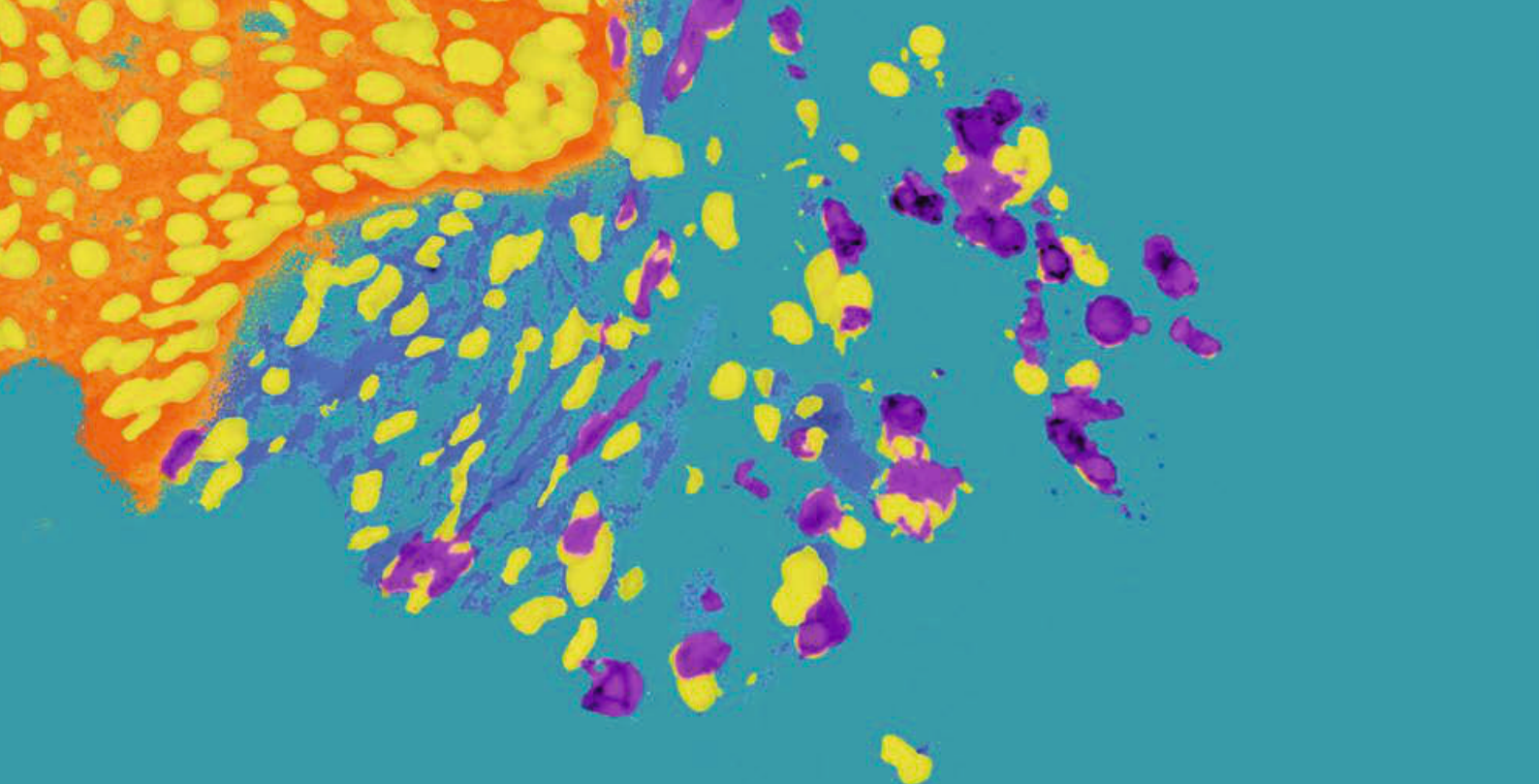
MACSwell Imaging Frames can be attached to any standard microscope slide and provide the reaction cavity needed for a MICS experiment. These frames come in different sizes, ensuring a perfect fit for your tissue sample. To achieve even higher resolution, utilize our MACSwell HighRes slides, featuring a 170  $\mu\text{m}$  thin glass bottom for exceptional detail capture.

### ADHERENT CELLS

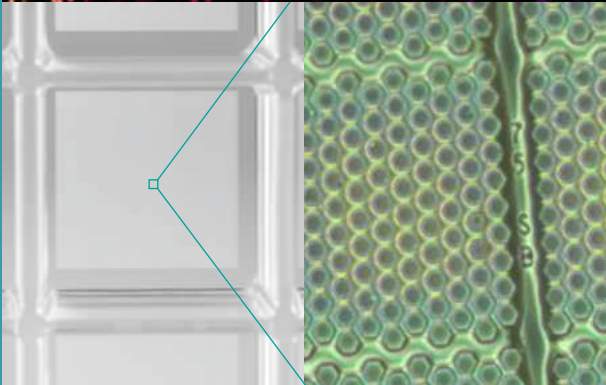
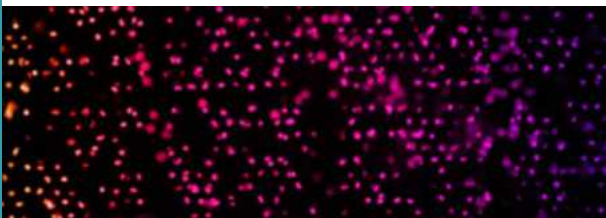


### MACSwell 24 Imaging Plates

MACSwell 24 Imaging Plates come with 24 rectangular wells and a clear, 170  $\mu\text{m}$  thick glass bottom. Just pipette your cell suspension onto the plate, culture it as usual, and then follow your standard protocol to fix the sample directly on the plate.



## SUSPENSION CELLS

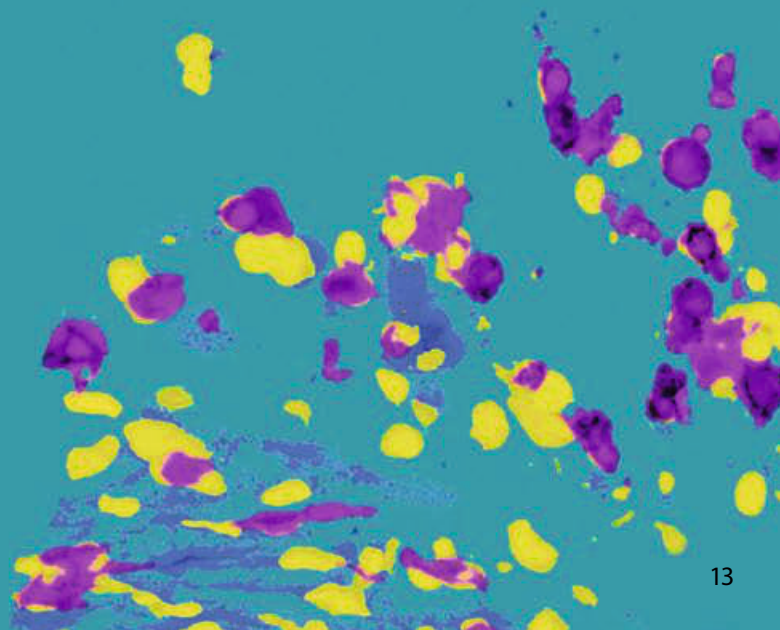


### MACSwell Sample Carriers with microcavities

MACSwell 24 Micro Imaging Plates feature hundreds of thousands of hexagonal microcavities, each perfectly fitting one cell. Just pipette your suspension cells into one of the 24 wells, wash, and proceed to analyze your perfectly singularized suspension cells.

### Validated fixation methods

- ✓ Formalin-fixed paraffin-embedded (FFPE)
- ✓ Frozen (PFA or acetone-fixed)



# Pretested antibodies for MICS

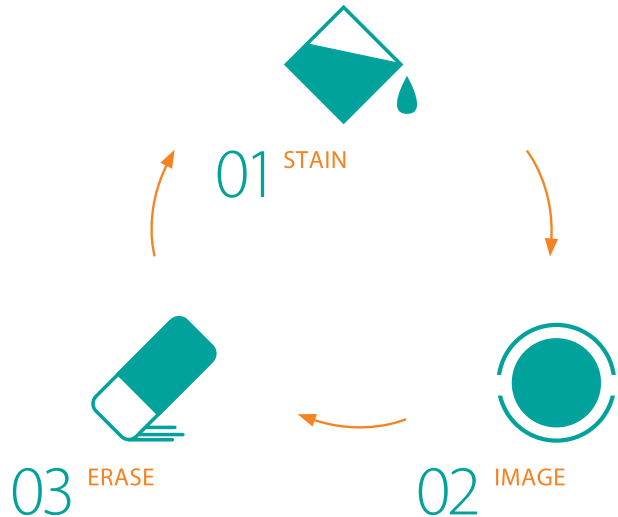
## Specific staining – conclusive results

To achieve reliable and error-free analyses, rely on the world's largest portfolio of primary conjugated antibodies for spatial biology:

- Pretested for MICS technology on the MACSima Platform, to be compatible with FFPE or fixed frozen (PFA or acetone-fixed) samples of human or mouse origin
- Recombinantly engineered for high specificity
- Lot-to-lot consistent, ensuring reproducible results over time

### The two mechanisms for signal erasure

After staining with fluorochrome-conjugated antibodies (01) and image acquisition of the stained sample (02), the fluorescent signal can be erased (03) by one of the two mechanisms shown below.



The fluorescent signal of samples that were stained with fluorochrome-conjugated antibodies, such as our recombinant REAfinity® Antibodies coupled to non-photostable FITC, PE or APC fluorochromes, can be erased via photobleaching.

Staining of samples with REAdye\_lease™ and REAlease® Fluorochrome-Conjugated Antibody complexes allows for fast and gentle signal erasure via a controlled release of fluorochromes.



# Convenient antibody formats



Explore   
**600+**  
**antibodies**  
▶ [miltenyibiotec.com/  
MICS-antibodies](https://miltenyibiotec.com/MICS-antibodies)



## Antibody conjugates for MICS

Choose from a huge portfolio of antibodies pretested for MICS to fast and easily design the exact panel you need for your analysis.

Importantly, enjoy the flexibility to use your own or third-party antibodies for your MICS experiments as well, with the option to combine them seamlessly with Miltenyi Biotec antibodies within a single experiment.

## Antibody panels for MICS

Boost your research efficiency with ready-to-use antibody panels, pre-defined for various applications, saving you valuable time on method optimization. Choose from flexible REAplex Panels (liquid) or highly standardized REAscreen™ Panels (dried) for consistent results.

Need a custom solution? REAscreen Design allows for personalized dried panels, whether you need a large stock of a 30-marker panel or just a few replicates of a 100-marker panel.



# Same-section spatial multiomics

Our RNAsky™ Technology empowers you to complement your ultrahigh-plex spatial proteomics experiment with RNA transcript detection – all within the same tissue section. Leveraging Miltenyi Biotec’s MICS technology, gene expression of selected RNA targets can now be seamlessly incorporated into the comprehensive MACSima Workflow.

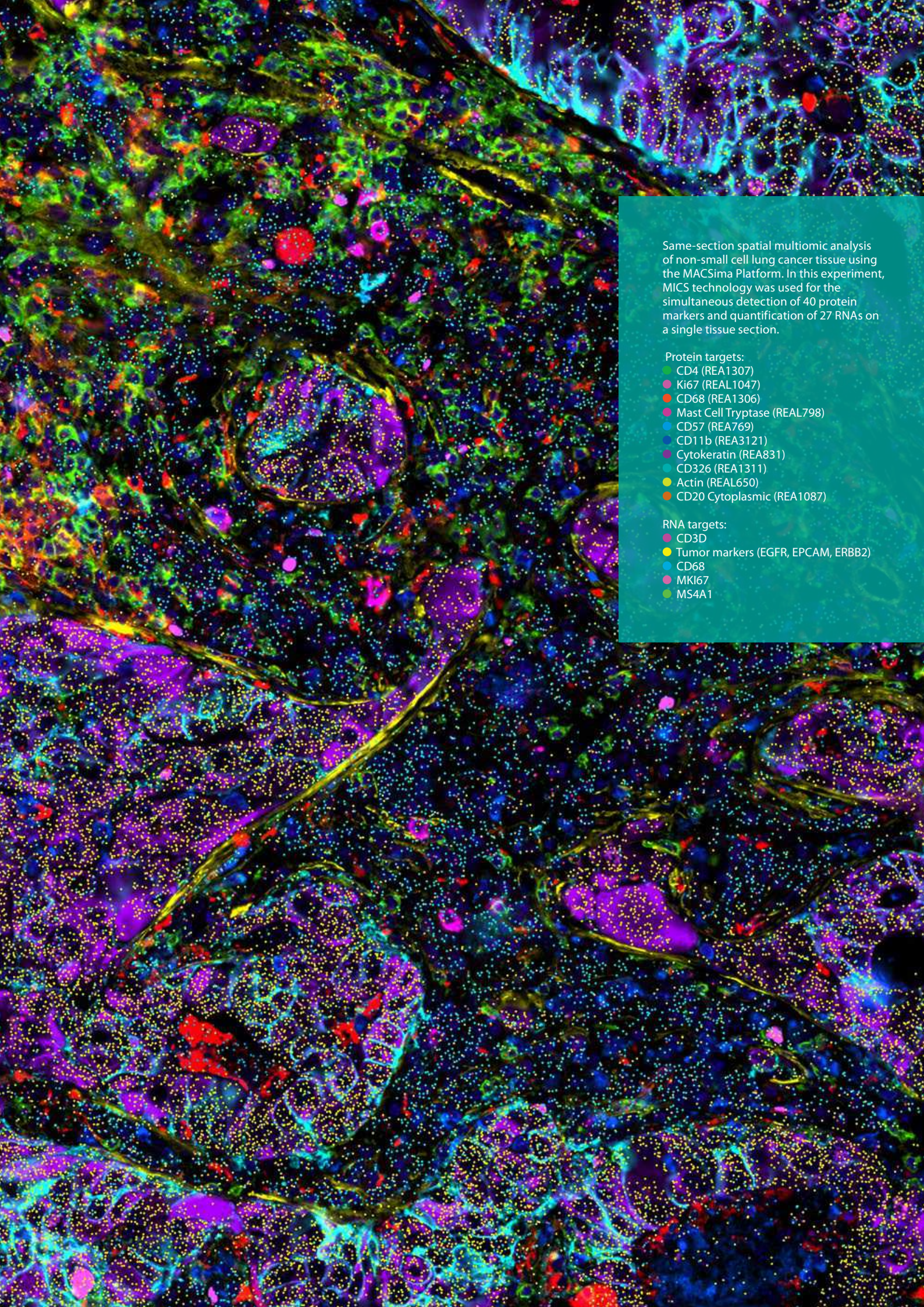
► [miltenyibiotec.com/RNAsky](https://miltenyibiotec.com/RNAsky)



Download our flyer on same-section spatial RNA and protein analysis.

► [miltenyibiotec.com/spatial-multiomics](https://miltenyibiotec.com/spatial-multiomics)





Same-section spatial multiomic analysis of non-small cell lung cancer tissue using the MACSima Platform. In this experiment, MICS technology was used for the simultaneous detection of 40 protein markers and quantification of 27 RNAs on a single tissue section.

Protein targets:

- CD4 (REA1307)
- Ki67 (REAL1047)
- CD68 (REA1306)
- Mast Cell Tryptase (REAL798)
- CD57 (REA769)
- CD11b (REA3121)
- Cytokeratin (REA831)
- CD326 (REA1311)
- Actin (REAL650)
- CD20 Cytoplasmic (REA1087)

RNA targets:

- CD3D
- Tumor markers (EGFR, EPCAM, ERBB2)
- CD68
- MKI67
- MS4A1

# MACS iQ View – Spatial Biology

Sophisticated yet simple analysis software



The MACS iQ View – Spatial Biology Software Package was specifically designed to manage and analyze the vast amount of valuable data generated by the MACSima Platform. Our primary goal in developing this software was to make spatial data analysis accessible to users from all backgrounds.

With MACS iQ View, handling and analyzing hundreds of images couldn't be simpler. You can easily display individual experimental markers or any combination you require. Efficiently organize your data using various display options and save your preferences to increase the consistency and reproducibility of your analyses.

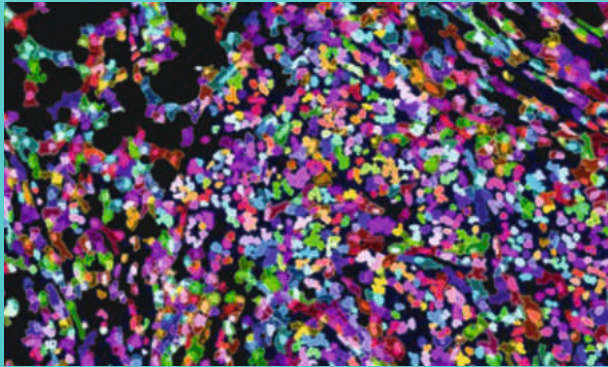
## Interactive and dynamic data display

The software's user interface is highly intuitive and easy to use. Interactive and dynamic gating or clustering enables you to view the results immediately in a variety of graphs, tables, and a vast array of plots.

Visit our website to learn more about  
MACS iQ View – Spatial Biology.

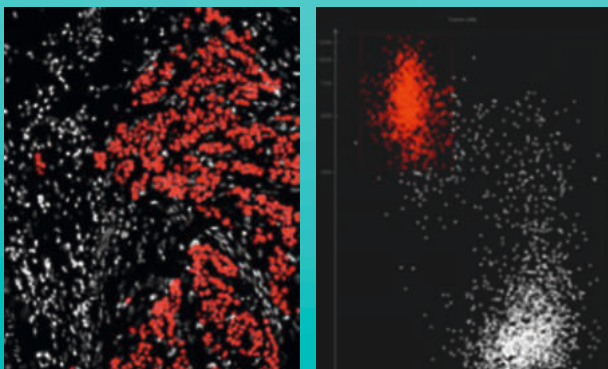
► [miltenyibiotec.com/MACS-iQ-View](https://miltenyibiotec.com/MACS-iQ-View)





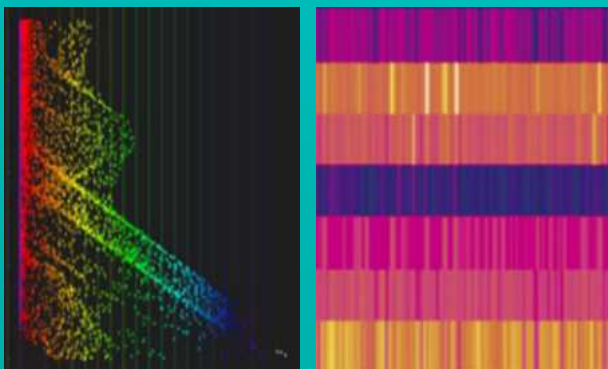
## Easy segmentation

Defining the cell and nucleus boundaries is an effortless task with MACS iQ View – Spatial Biology. You can begin your analysis quickly with simple definition of parameters and fast processing. Choose between various predefined segmentation options or conveniently import your own trusted segmentation mask.



## Multifaceted gating and clustering enable deep phenotyping

Deep phenotyping can be achieved through highly interactive, dynamic manual gating both on the graph and the image. A workflow editor lets you keep track of all selection steps. You can also use the integrated clustering options according to the features of your interest. All this allows you not only to phenotype the cells, but to also view their position on the image and analyze spatial relationships and more.



## Cutting-edge analysis and plotting options for clear data display

MICS data enable you to examine tissue samples and cells in great detail. To display the high-dimensional data on the cells' complex phenotypes and spatial organization in an easy-to-grasp way, the software offers sophisticated analysis tools. Dimension reduction plots (t-SNE and UMAP), distance mapping, and a range of additional display options, such as heatmaps, let you visualize your intricate data.



## Turn spatial data into discoveries

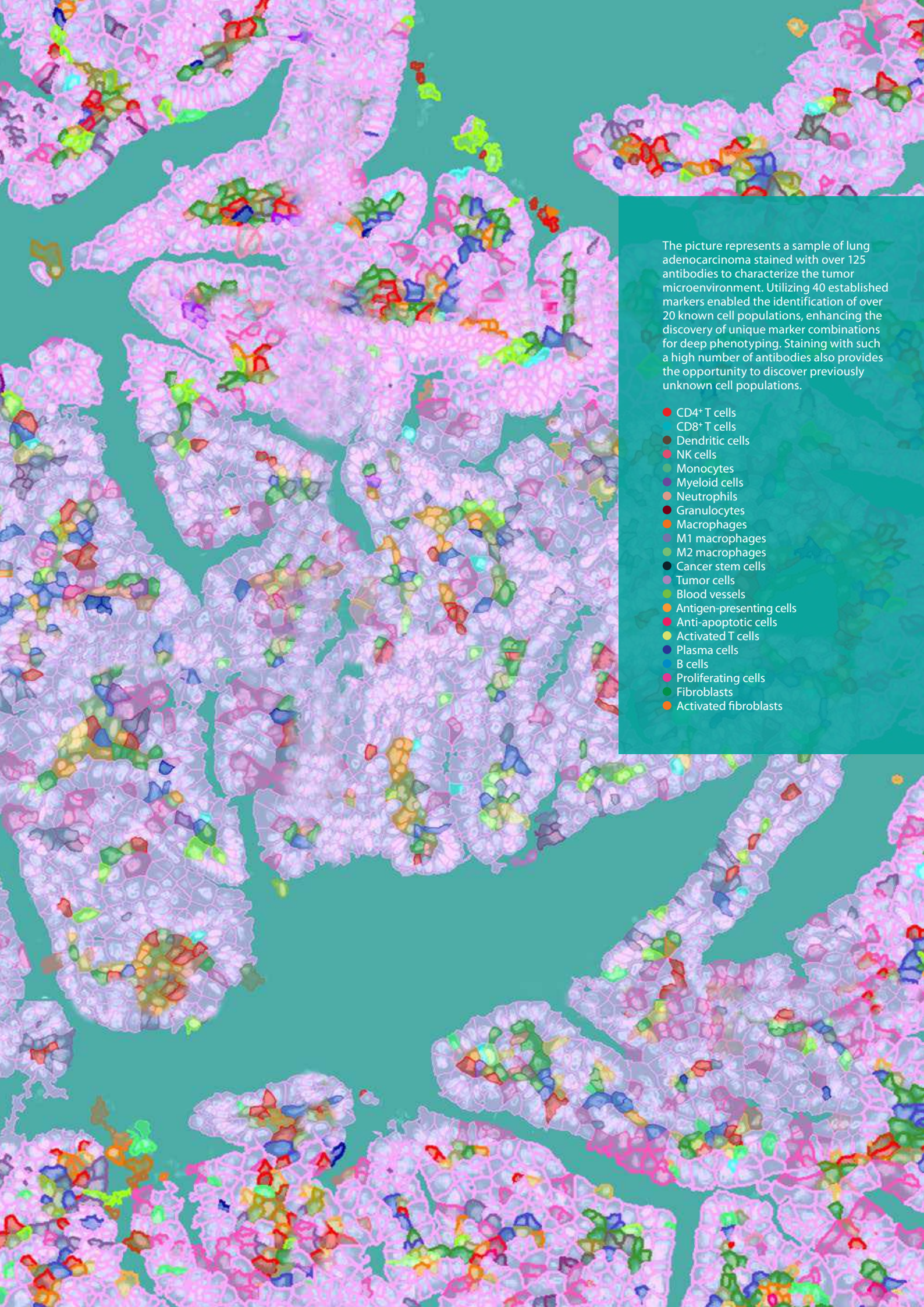
Experience what highly multiplexed imaging based on MICS technology can bring to your research. The possibilities with spatial biology are endless and you can bring new discoveries to light that could revolutionize the study of disease characterization and the development of new therapies.

► [miltenyibiotec.com/MACSim](https://miltenyibiotec.com/MACSim)

Download our application note to learn more about the analysis of the tumor microenvironment in lung adenocarcinoma.

► [miltenyibiotec.com/MACSim-lung-TME-appnote](https://miltenyibiotec.com/MACSim-lung-TME-appnote)





The picture represents a sample of lung adenocarcinoma stained with over 125 antibodies to characterize the tumor microenvironment. Utilizing 40 established markers enabled the identification of over 20 known cell populations, enhancing the discovery of unique marker combinations for deep phenotyping. Staining with such a high number of antibodies also provides the opportunity to discover previously unknown cell populations.

- CD4<sup>+</sup> T cells
- CD8<sup>+</sup> T cells
- Dendritic cells
- NK cells
- Monocytes
- Myeloid cells
- Neutrophils
- Granulocytes
- Macrophages
- M1 macrophages
- M2 macrophages
- Cancer stem cells
- Tumor cells
- Blood vessels
- Antigen-presenting cells
- Anti-apoptotic cells
- Activated T cells
- Plasma cells
- B cells
- Proliferating cells
- Fibroblasts
- Activated fibroblasts

# One experiment, endless discoveries



## Deep phenotyping

By examining hundreds of protein markers in their spatial context, researchers can uncover intricate details about cell heterogeneity, microenvironment interactions, and disease-specific patterns, ultimately advancing our knowledge of complex biological systems.



## Biomarker research and discovery

The correlation between various markers in your sample is vital for uncovering biomarker signatures. This understanding plays a pivotal role in developing patient stratification strategies and innovative therapies tailored to individual needs, revolutionizing the treatment of numerous diseases.



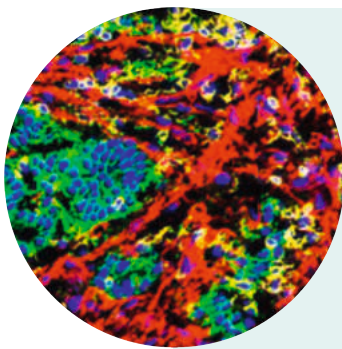
## Drug target discovery and validation

By conducting spatial analysis with a wide range of markers, you can identify potential drug development targets. Using the MACSima Platform, these candidates can be further assessed and validated in preclinical research studies, considering the comprehensive microenvironment. This approach can enhance the accuracy and depth of drug effectiveness analysis.

# Where every marker tells a story

Thoroughly analyzing a wide range of markers not only boosts your current research but also creates a valuable archive for addressing future questions, even those you haven't thought of yet. You can revisit datasets from your MICS experiments anytime to uncover new insights.

Your spatial data holds unlimited potential for discoveries. Explore how other researchers used the MACSima Platform in their groundbreaking research in the examples below.

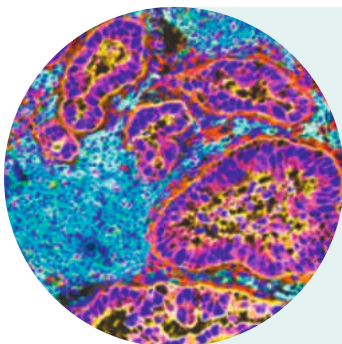


## Spatial single-cell atlas of the liver

MICS technology helped researchers to generate a cellular atlas of the entire human and murine liver.

Read the paper in Cell.

► [cell.com/cell/fulltext/S0092-8674\(21\)01481-1](https://cell.com/cell/fulltext/S0092-8674(21)01481-1)

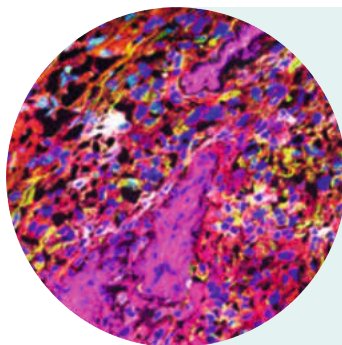


## Identification of target candidates for CAR T cell-based immunotherapy of pancreatic adenocarcinoma

Pancreatic ductal adenocarcinoma samples were fixed with acetone and screened based on 107 markers.

Read the publication in Nature Communications.

► [nature.com/articles/s41467-021-21774-4](https://nature.com/articles/s41467-021-21774-4)



## New potential target pair for CAR T cell treatment of solid tumors

In this publication, more than 300 antibodies were applied to analyze a single PFA-fixed tissue sample.

Read the full story.

► [nature.com/articles/s41598-022-05841-4](https://nature.com/articles/s41598-022-05841-4)



Delve into cutting-edge spatial biology research with the MACSima Platform.

► [miltenyibiotec.com/MACSima-publications](https://miltenyibiotec.com/MACSima-publications)



# All you need for spatial biology excellence

## MACSima Platform specifications

### Microscope

Instrument type	Widefield epifluorescence microscope
Camera	Equipped with a latest-generation sCMOS camera with high resolution and thermoelectrically cooled sensor (15 megapixel, large 25 mm diagonal field of view)
Excitation	Six high-power excitation LEDs (filters: 386/23 nm, 420/10 nm, 470/40 nm, 531/46 nm, 628/32 nm, 725/40 nm)
Emission	Five emission filters (470/40 nm, 530/43 nm, 580/25 nm, 698/70 nm, 809/81 nm)
Autofocus	Dual approach of hardware- and image-based autofocus mechanisms
Objectives	<ul style="list-style-type: none"> <li>• 2× objective to generate overview images; NA 0.1</li> <li>• 20× long working distance objective (designed for 1 mm thick slides); NA 0.45</li> <li>• 20× objective with high numerical aperture (designed for 170 µm thick cover glass); NA 0.75</li> </ul>
Bleaching unit	<ul style="list-style-type: none"> <li>• Separate bleaching unit for optimized signal erasure</li> <li>• Illuminated area: 3 mm × 3 mm</li> <li>• Light intensity: 2 W</li> </ul>

### Liquid handling system

Needle arm	Robotic needle arm allowing fully automated liquid transfer
Steel needle	Washable stainless steel needle with minimized spillover
Syringe pump	Syringe pump drive for accurate volumetric staining of samples
Fluid containers	1.5 L fluid containers for automatic operation over several days without the need to exchange containers

### Sample and reagent stage

Automated stage	Stage with sub-micron positioning accuracy of 100 nm (automated image registration for different cycles)
Automated sample and reagent carrier positioning	Convenient loading and clamping of all supported sample carriers and reagents

### Technical data

Computer	Two integrated computers for experiment planning/execution and image analysis
Monitors	<ul style="list-style-type: none"> <li>• Tiltable integrated touch display (Full HD) for PC1</li> <li>• External 4K monitor for PC2</li> </ul>
Storage/ports	<ul style="list-style-type: none"> <li>• 25 TB integrated storage to store data of several experiments</li> <li>• 2× USB 3.0</li> <li>• HDMI port</li> </ul>
Network	1× 10 GbE 1× RJ45 GbE/10GbE
Power requirement and consumption	100–240 V, 50/60 Hz, max. 7/13A, max. 1,300 W

### MACS iQ View Software

Control software	<ul style="list-style-type: none"> <li>• Comprehensive sample and reagent management system</li> <li>• Easy planning and design of both simple and complex experiments</li> <li>• User-friendly execution and monitoring of experiments</li> </ul>
Analysis software (Spatial Biology Package)	<ul style="list-style-type: none"> <li>• Easy display of hundreds of markers from high-dimensional datasets</li> <li>• Fast and flexible segmentation</li> <li>• Interactive gating</li> <li>• Unbiased data analysis (k-means clustering, UMAP and t-SNE calculation)</li> <li>• Multiple plotting options (histogram, scatter plot, strip and violin plots, heatmaps)</li> <li>• Workflow editor</li> <li>• Distance analyses</li> </ul>

### Size and weight

Dimensions	<ul style="list-style-type: none"> <li>• Instrument dimension: 1,220 mm × 780 mm × 650 mm (w × d × h); footprint: 1,210 mm × 750 mm (w × d)</li> <li>• MACSima Table<sup>1</sup>: 1,250 mm × 765 mm × 813 mm (w × d × h)</li> </ul>
Weight	<ul style="list-style-type: none"> <li>• Instrument: 170 kg</li> <li>• MACSima Table<sup>1</sup>: 120 kg</li> </ul>

Product type	Order no.
<b>Instrument</b>	
MACSima System	130-121-164
MACSima Table	150-001-781
MACSima 4K monitor	150-001-775
<b>Software</b>	
<b>Licences for MACS iQ View – Spatial Biology<sup>2</sup></b>	
<ul style="list-style-type: none"> <li>• Annual license</li> <li>• Permanent license</li> </ul>	
<b>Antibodies and reagents</b>	
<b>MICS-prettested antibody conjugates<sup>3</sup></b>	
<ul style="list-style-type: none"> <li>• REAfinity Recombinant Antibodies</li> <li>• REA dye_release Releasable Fluorochromes</li> <li>• REAlease Releasable Antibodies</li> </ul>	see website
<b>Pre-defined Antibody Panels for MICS<sup>3</sup></b>	
<ul style="list-style-type: none"> <li>• REAscreen™ Immuno-oncology Kit, human, FFPE</li> <li>• REAscreen MAX Kit, human, PFA</li> <li>• REAscreen MAX Kit, human, PFA</li> <li>• REAscreen MAX Kit, mouse, PFA</li> </ul>	see website
<b>Support Reagents for MICS</b>	
<ul style="list-style-type: none"> <li>• MACSima Stain Support Kit, human</li> <li>• MACSima Stain Support Kit, mouse</li> </ul>	130-127-574 130-127-575
<b>Sample carriers<sup>4</sup></b>	
MACSwell One Imaging Frames	
MACSwell One Small Imaging Frames	
MACSwell Two Imaging Frames	
MACSwell Four Imaging Frames	
MACSwell 24 Imaging Plates	see website
<b>Buffers and accessories</b>	
MACSima Buffer Starting Kit	130-125-753
MACSima Running Buffer 6×1.5 L	130-121-565
MACSima System Buffer 6×1.5 L	130-125-315
MACSQuant®/MACSima Storage Solution 6×1.5 L	130-092-748
MACSwell Deepwell Plates	130-126-865
MACSwell Sealing Foils	130-126-866

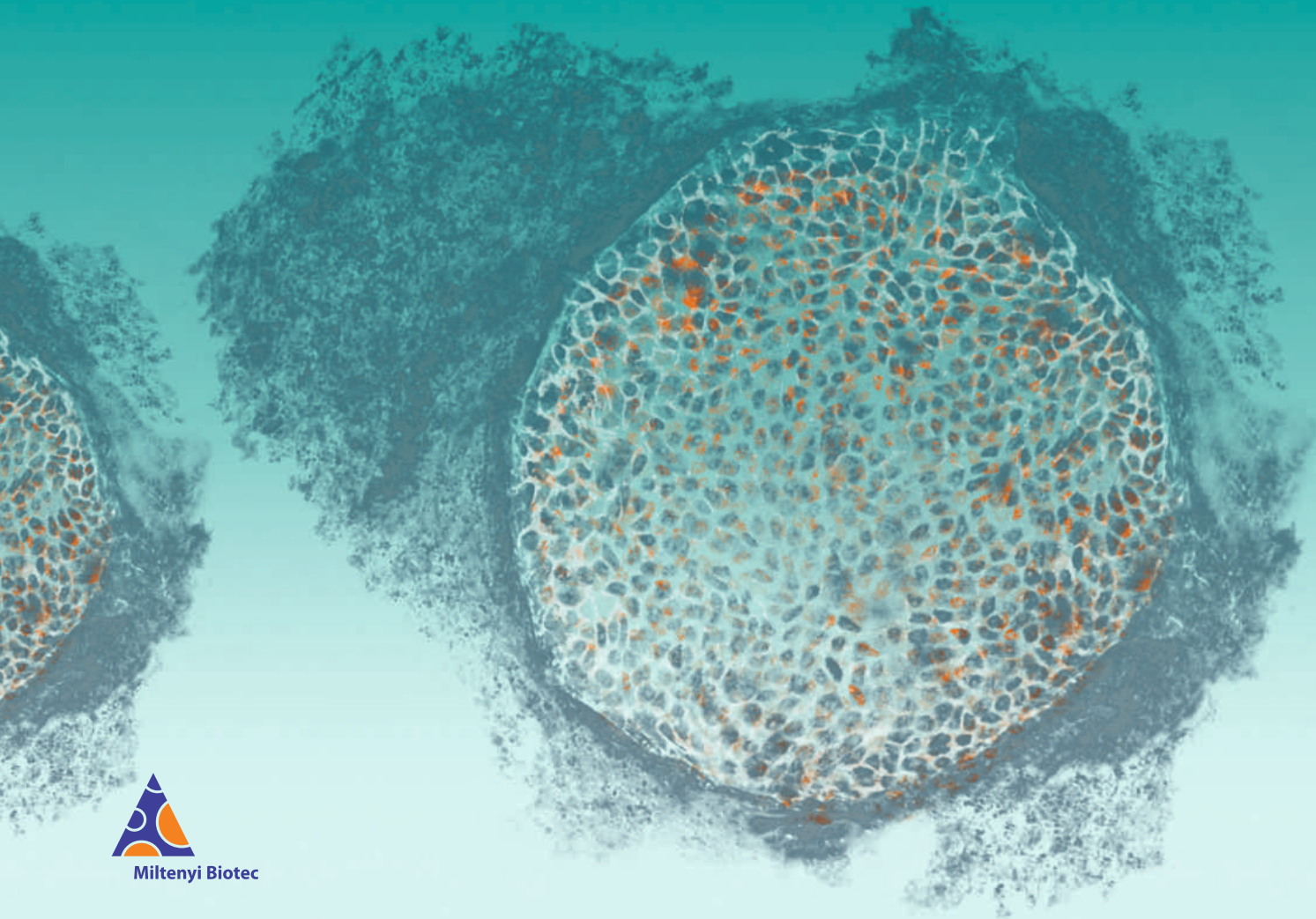
<sup>1</sup> The MACSima System is delivered with a trolley table specifically designed to support the system. It has anti-vibration properties and provides a closed storage compartment.

<sup>2</sup> For detailed information about the different license options, visit [miltenyibiotec.com/MACS-iQ-View](https://miltenyibiotec.com/MACS-iQ-View)

<sup>3</sup> For details on the wide range of Miltenyi Biotec antibodies for MICS, visit [miltenyibiotec.com/MICS-antibodies](https://miltenyibiotec.com/MICS-antibodies)

<sup>4</sup> For more information about the latest sample carriers from Miltenyi Biotec, visit [miltenyibiotec.com/MICS-sample-carriers](https://miltenyibiotec.com/MICS-sample-carriers)

► [miltenyibiotec.com/MACSima](http://miltenyibiotec.com/MACSima)



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