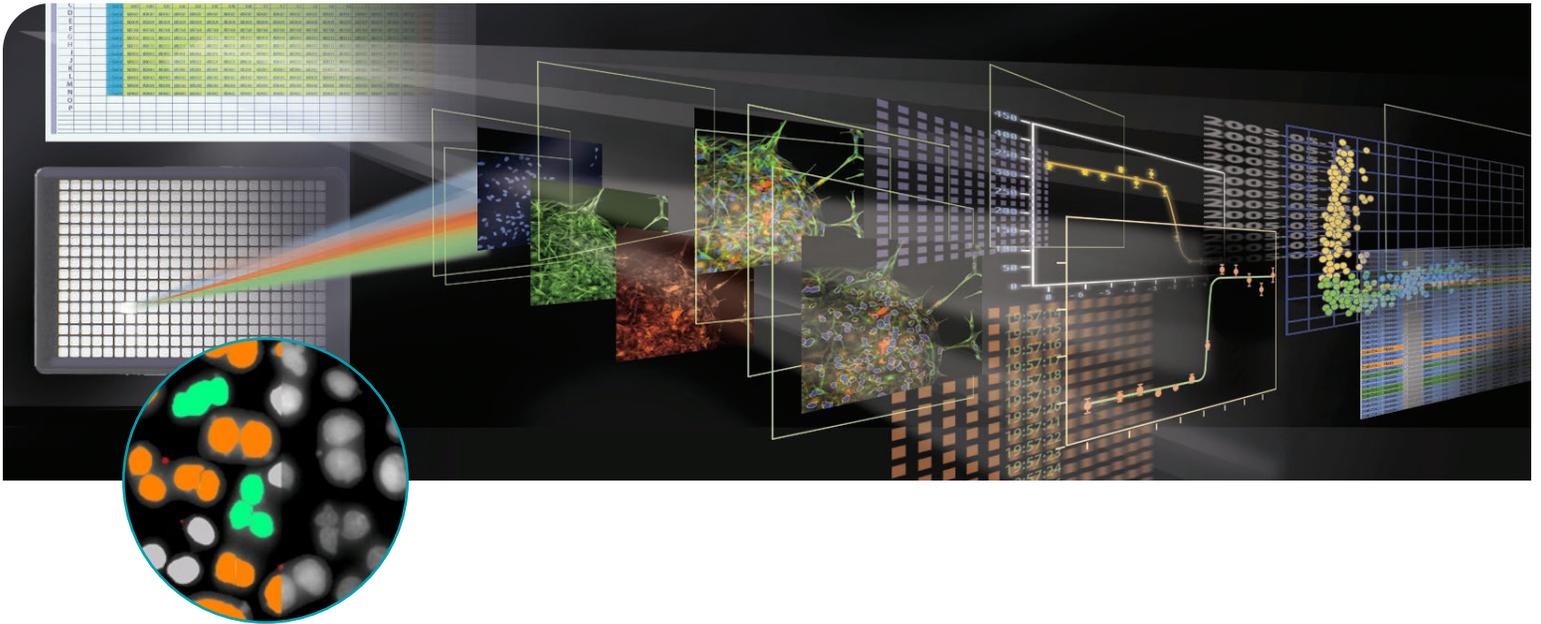


MetaXpress Software Micronuclei Application Module

ANALYSIS DROP-IN FOR METAXPRESS SOFTWARE AND METAXPRESS POWERCORE HIGH-THROUGHPUT IMAGING OPTION



- CLASSIFY MICRO- AND MULTI-NUCLEATED CELLS
- ADDITIONAL MARKERS FOR ANALYSIS OF CYTOTOXICITY
- SUPERIOR SEGMENTATION ALGORITHMS AND ADAPTIVE BACKGROUND CORRECTION
- MORE THAN 100 OUTPUTS AND CUSTOMIZATION THROUGH METAXPRESS SOFTWARE MACROS
- FASTEST ACQUISITION-THROUGH-ANALYSIS WORKFLOW WITH ON-THE-FLY COUNTING OF CELLS
- COMPATIBLE WITH METAXPRESS POWERCORE HIGH-THROUGHPUT IMAGE ANALYSIS OPTION

Micronuclei are small nuclei produced during cell division by a lagging chromosome fragment or entire chromosome. Detection of micro- and multi-nucleated cells is an accepted and stringent method to screen for indicators of genetic toxicity early in drug discovery. Automated detection of these structures is one of the most demanding image analysis applications.¹ Superior segmentation algorithms are required to analyze the wide range of phenotypes produced upon extended treatments. In addition, both image acquisition and analysis need to be performed at very high speed to detect these rare events in large compound libraries.

The MetaXpress[®] Software Micronuclei Application Module from Molecular Devices compliments the suite of existing cell toxicology application modules, which includes cell cycle analysis, cell health profiling, live/dead determination, and mitotic index calculation. The module is easy to use and advances micronuclei and genotoxicity analysis through a proprietary algorithm to define mono- and multi-nucleated cells as well as identify micronuclei. It also features the fastest image acquisition and analysis through integration with Molecular

Devices' complete solution for cellular imaging:

- ImageXpress[®] High-Content Imaging Systems
- MetaXpress[®] PowerCore[™] Software for high-throughput image analysis
- AcuityXpress[™] Software for quality control and data analysis

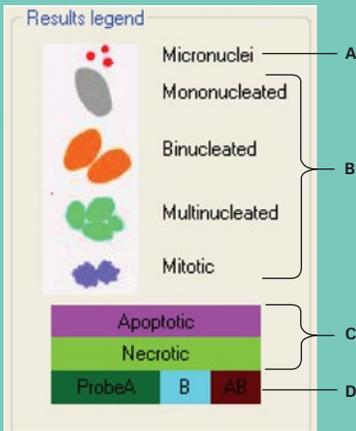
SUPERIOR SEGMENTATION AND 100+ OUTPUTS Easily discriminate mono- and multi-nucleated cells:

The proprietary algorithm used in the MetaXpress Software Micronuclei Application Module offers advanced segmentation of mono-, bi-, and multi-nucleated cells without the use of a cytoplasmic marker. Using only a nuclear probe, this validated method reduces sample preparation time while increasing throughput of image acquisition and analysis when compared to traditional techniques.

Highly configurable detection of micronuclei:

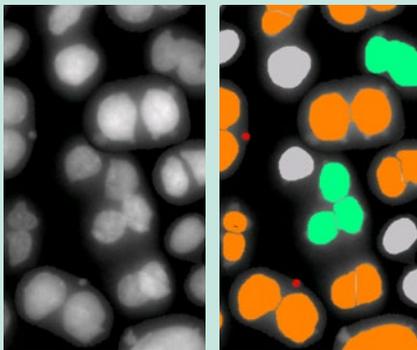
Micronuclei can be quantified in all the above-mentioned cellular classifications. They can be defined by their size, intensity, and distance from the main nucleus, allowing distinction of micronuclei from "buds" or "blebs."

Easy Assay Setup and Optimization



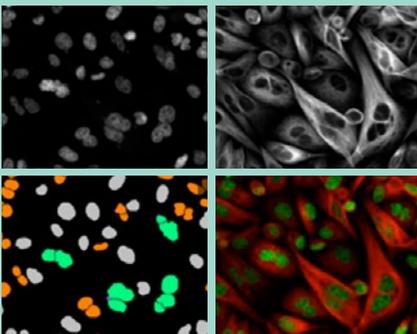
More than 100 parameters from these classifications help determine genotoxicity, proliferative status, cytotoxicity, and others. Custom analysis can be added using MetaXpress software macros. **A:** Identification of Micronuclei; **B:** Mono-/bi-/poly-nucleated or mitotic cell classification with a single DNA stain; **C:** Further definition of cytotoxicity with stains for apoptosis or necrosis; **D:** Option for two more "custom" markers (e.g. cell type-specific or transfection markers).

Superior Micronuclei Detection



Images of cells before (left) and after (right) image segmentation with the MetaXpress Software Micronuclei Application Module.

Segmentation of Mono-, Bi-, and Poly-Nucleated Cells Without a Cytoplasmic Stain



The MetaXpress Software Micronuclei Application Module allows segmentation of multi-nucleated cells. Acquired images with only a nuclear stain (top left) are processed using Molecular Devices' proprietary algorithm. The segmentation results (bottom left) are comparable to traditional methods requiring both nuclear and cytoplasmic stains (top right shows the cytoplasm only and bottom right merges nuclear and cytoplasmic markers). Data courtesy of Dr. Stefan Prechtel, Bayer Schering Pharma.

Measure cytotoxicity and cell proliferation with a nuclear stain: Since micronucleus expression is dependent on cell proliferation, quantification of cell proliferation and death can be carried out simultaneously to obtain a sound evaluation of cell kinetics and micronucleus frequencies. A wide range of output, including nuclear division index, are available with only one nuclear probe.

Additional probes for cytotoxicity and other key markers: To allow for further distinction of cytotoxicity, the module features an option to measure to four additional probes: apoptotic, necrotic and two custom probes (for example, cell type-specific or transfection markers).

Adaptive Background Correction: Similar to other MetaXpress Software application modules, the Adaptive Background Correction feature adapts the nuclear detection to the local intensity ranges and shape features within and between cells to provide the most robust segmentation available in an image-based screening system.

And more: Nuclei cut by the edge of an image can easily be excluded during analysis using the "Exclude border nuclei" option. For all probes, areas and intensities are available along with a full suite of multi-parametric information. All data is available at a cell-by-cell or image-by-image level. Once the analysis is run, a cellular results table allows interactive reviewing of individual cellular measurements.

FURTHER CUSTOMIZATION THROUGH MACROS MetaXpress Software and the Micronuclei Application Module are seamlessly integrated with the flexibility of MetaMorph® Software and its advanced automation macros. These powerful macros record and perform a series of tasks without the user having to know a programming language.

THE FASTEST WORKFLOW FROM ACQUISITION TO HIT SELECTION

Image acquisition with ImageXpress Systems provides the fastest read times for large libraries and great flexibility in acquisition set-up for research through screening. On-the-fly cell counting ensures a pre-defined number of cells is captured and decreases image acquisition times.

Image analysis can be distributed to the MetaXpress PowerCore high-throughput image analysis platform, providing unparalleled performance in the race to identify "hits." Increasing image analysis speed by 10-to 30-fold virtually eliminates image analysis bottlenecks and enables multiple ImageXpress systems to run in parallel.

High-end hit selection and quality control is available through AcuityXpress Software, the data analysis software integrated in Molecular Devices' complete imaging solution. AcuityXpress Software features an interactive drill down for bidirectional interaction between images and numerical data.

ORDERING INFORMATION

MetaXpress Software Micronuclei Application Module
Part Number: 9500-0045

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1. Michael Fenech, "Cytokinesis-Block Micronucleus Cytome Assay", *Nature Protocols*, 1084, Vol. 2 No. 5 (2007).

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