

Automation of Genetic Toxicology Tests

Customizations for
Toxicology



Versatile Applicability

With Metafer, the analysis of all major microscope-based preclinical tests in genetic toxicology can be partly automated. Our customization packages comply with the OECD guidelines of the respective tests and can be designed to be fully GLP-compliant.



Established Sensitivity

Many laboratories worldwide benefit from Metafer imaging automation in genetic toxicology. Together with our long-term users, the parameter sets for all tests could be developed and optimized in a practice-oriented way.



High Specificity

Standardization is key to genetic toxicology testing. The often very subtle effects can only be reliably detected if all aspects of the test, including the scoring, are performed on the basis of standardized parameters.

METAFER
TOXICOLOGY
AUTOMATION

Outstanding Speed

MetaSystems offers hardware extensions that work seamlessly with the Metafer software allowing for high scanning speed and excellent image quality. For instance, a typical cytokinesis block micronucleus slide is scanned in less than 4 minutes.



Adaptive Scalability

An imaging system operated by Metafer has a modular design and is easy to adapt to individual needs. Customization packages can be combined with each other as desired, and the slide capacity ranges from 8 to 800 preparations per run.









Seamless Integration

Each Metafer installation comes with Neon, a study and image management tool that provides users with a clear overview of all results. Data, images, and statistical results can be exchanged manually or automatically with other databases.



Customizations - Overview

| Customization Package | Guideline | GLP | Main Functionality |
|--|-----------|-----|---|
|  Chromosomal Aberration Assay | #473 | Yes | Automated imaging; manual on-screen analysis. |
|  Cytokinesis-Block Micronucleus Test | #487 | Yes | Unattended MN scoring in bi-nucleates. |
|  Proliferation Index (CBPI) | | | Automated CBPI calculation. |
|  Rodent Erythrocyte Micronucleus Test | #474 | Yes | MN scoring in PCE; PCE/NCE ratio. |
|  Single Cell Gel Electrophoresis | #489 | Yes | Fully automated analysis (TM, OTM, more). |
|  Ames II / Ames MPF Test | #471 | Yes | Colorimetric readout and colony detection. |

Metafer screen with the readout of the Rodent Erythrocyte Microcnuleus Test. Gallery shows the single objects detected. Histogram and figures summarize the measurement results and the distribution of PCE and NCE cell populations.



CONVENTIONAL TESTS

Chromosomal Aberration Assay

The Gold Standard

Although testing for chromosomal aberrations is intricate and manual analysis can be laborious, it remains the „Gold Standard“ for evaluating DNA damage.

With Metafer, users gain access to numerous tools that expedite and standardize the analysis process.

Benefits

- Automated metaphase finder and high-resolution imaging of metaphases,
- On-screen aberration analysis with customizable scoring sheets,
- Digital reporting and data export,
- Offline review installations for work-sharing evaluation,
- Comprehensive documentation of all findings and audit trails,
- High-volume scanning with up to 800 slides per run.

Comet Assay

Single Cell Gel Electrophoresis

The Comet assay measures DNA fragmentation in single cells, offering the benefits of speed, cost-effectiveness, and high sensitivity. However, it is susceptible to factors affecting reproducibility and requires imaging techniques to be analyzed.

Automating and standardizing the imaging procedure is crucial for enhancing the test's reliability and significance.

Benefits

- Automated selection of target cells based on morphology criteria,
- Assessment of all relevant cell features (e.g., tail moment, tail moment Olive, %DNA in tail, etc.),
- Documentation of all cells with graphical display of the results,
- Optionally: detection and separate assessment of „Hedgehog“ cells.

Ames Test

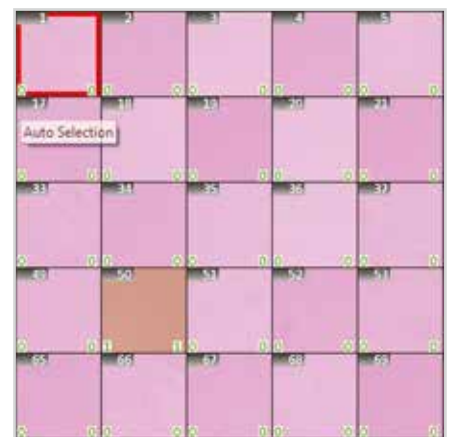
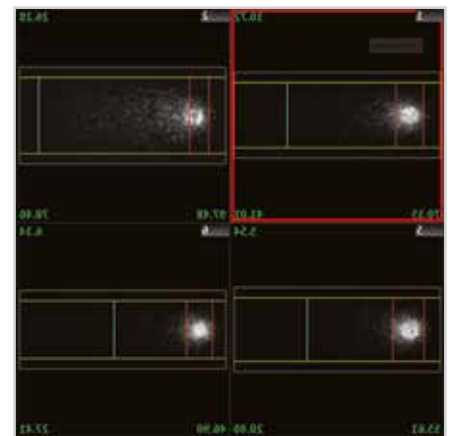
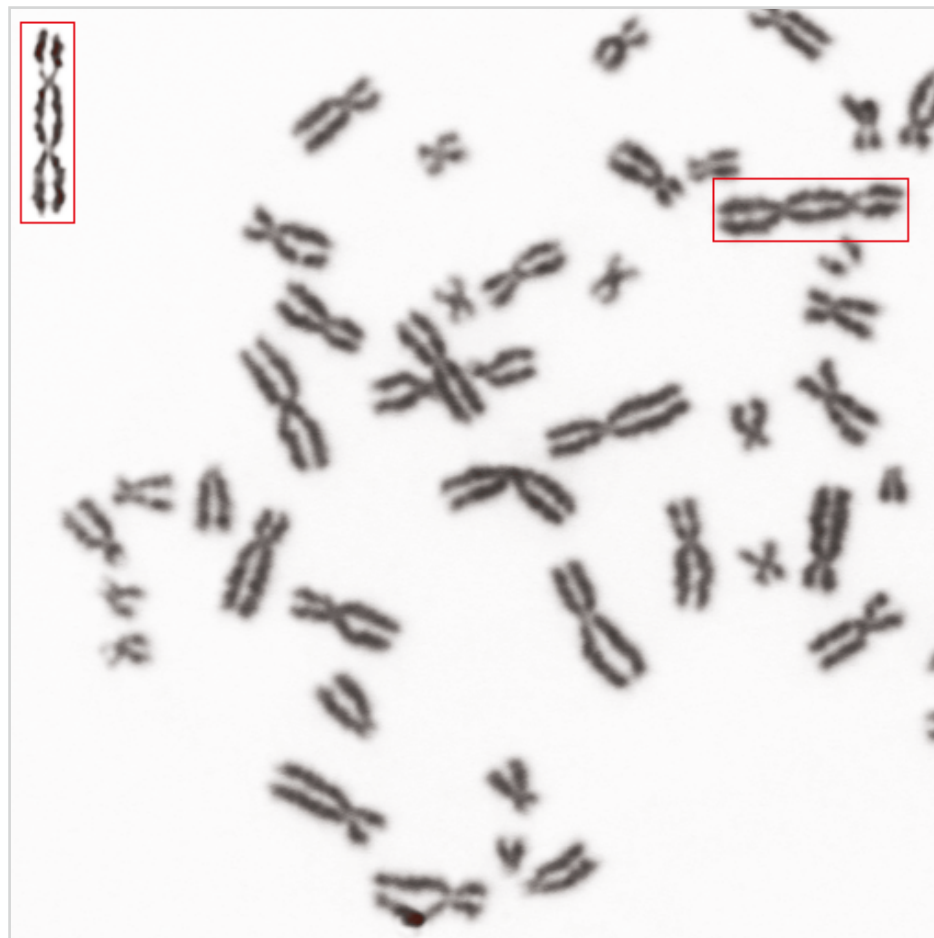
Ames II / MPF Assays

The Ames test is one of the earliest recognized methods in genetic toxicology. Its modern versions, Ames II and Ames MPF, utilize liquid cultures instead of agar plates and are conducted on 384-well plates with colorimetric readouts.

Metafer enhances these assays by using rapid imaging to detect positive cultures based on their color, and results are compiled into reports according to the test manufacturer's specifications.

Benefits

- Fast evaluation of individual wells (only one image per well required),
- Identification of positive cultures based on color values,
- Documentation according to the manufacturer's specifications as a report,
- Normal preparations and MWP can be scanned on the same device w/o conversion,
- High-volume scanning with up to 800 slides per run.



MICRONUCLEUS TESTS

Rodent Erythrocytes Micronucleus Test

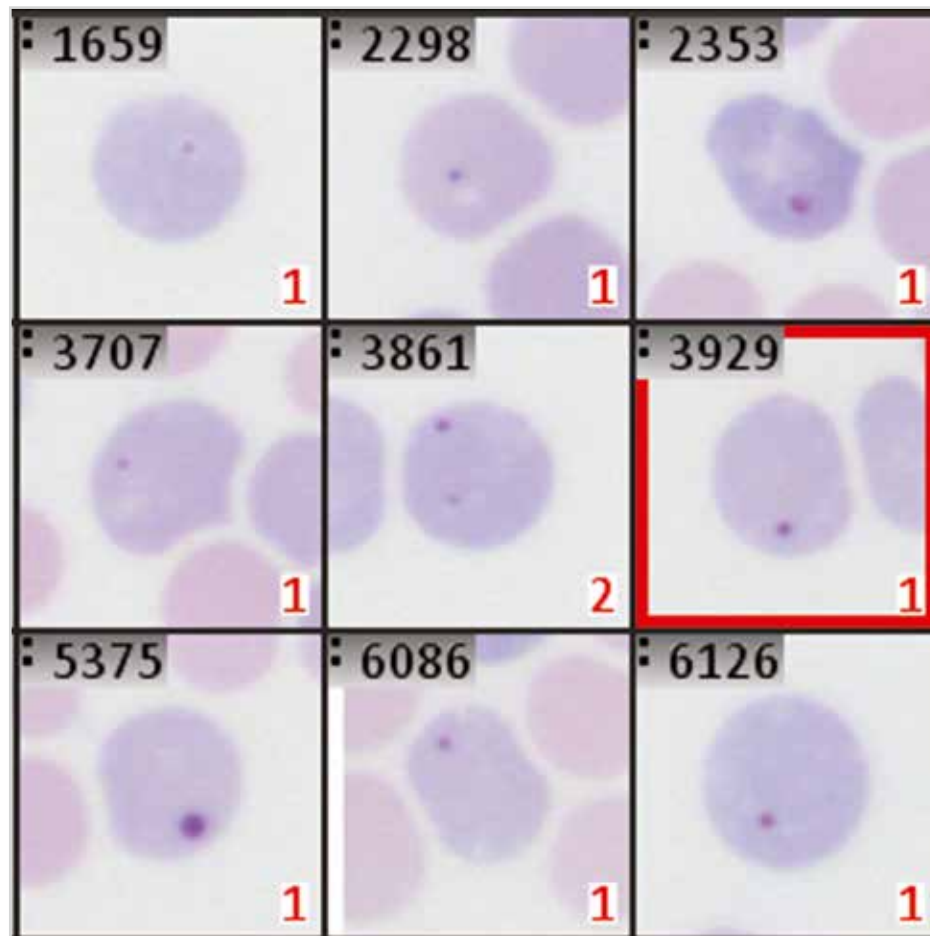
In Vivo Micronucleus Test

The Rodent Erythrocyte Micronucleus Test is commonly used for in vivo chemical evaluation, targeting immature erythrocytes (PCE) from animal bone marrow. It also assesses cytotoxicity by measuring the ratio of PCE to mature erythrocytes (NCE).

Metafer automates the entire test evaluation in compliance with OECD standards and GLP conditions.

Benefits

- Fully automated analysis of the test in May-Gruenwald-stained, purified erythrocyte samples,
- Automated calculation of micronucleus rates and PCE/NCE ratio,
- Documentation of each erythrocyte as gallery image,
- Automatic adjustment to staining variations.



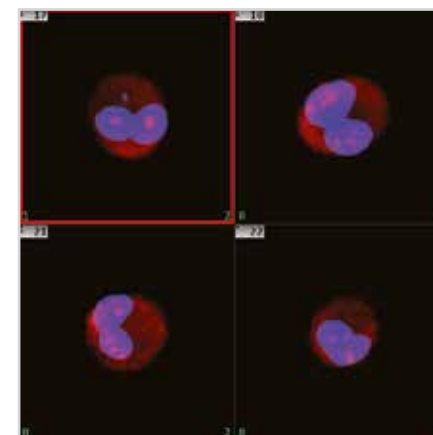
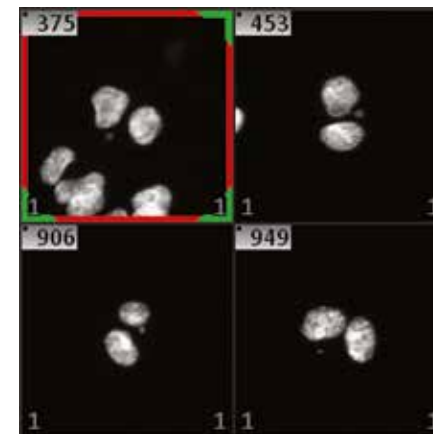
Cytokinesis-Block Micronucleus Test

Fast Assessment

Scoring micronuclei in bi-nucleated cells has been recognized as a fast and simple alternative to the aberration assay. Its straightforward analysis makes it ideal for full automation.

Benefits

- Ultra-fast imaging of DAPI stained micronucleus assay samples,
- Automated scoring of micronuclei in bi-nucleates or mononucleates,
- Digital reporting and data export,
- Smart review workflow with option to correct automated scoring proposals,
- Image gallery and quick relocation of all cells.



Proliferation Index (CBPI)

Cytotoxicity

The OECD guideline #487 for the mammalian cell micronucleus test recommends evaluating the Cytokinesis-Block Proliferation Index (CBPI) to determine cytotoxicity levels.

With a customization of a Metafer installation, this step can also be automated.

Benefits

- Automated assessment of mono-, bi-, and multinucleates,
- Automated calculation of the CBPI,
- Quick filter for the different cell classes,
- Image gallery and swift relocation of all cells.



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MetaSystems offers **Customization Packages** for application workflows that have been successfully implemented for customer labs using standard Metafer platform functionality. It is expected that they can be implemented for other customer labs using similar workflows and slide preparation procedures. If a Customization Package is purchased, MetaSystems product specialists will - based on their experience from other similar application cases - support the customer lab in adapting the Metafer software configuration to their needs. The performance of the solution will depend on the quality of the customer slides and the expertise of the users, MetaSystems cannot specify or guarantee any performance parameters. The validation of the solution for clinical use is the sole responsibility of the customer lab.

MetaSystems software provides, among other functions, features to assist users with image processing. These include, but are not limited to, the use of machine and deep learning algorithms for pattern recognition. The output generated in this process should be regarded as preliminary suggestions and, in any case, mandatorily requires review and assessment by trained experts.

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