EUROIMMUN Medizinische Labordiagnostika AG

EUROPattern Microscope

Computer-aided immunofluorescence microscopy (CAIFM)

- **Fully automated microscopy and modern diagnostics at the computer screen (cell substrates, tissues and EUROPLUS antigen dots, also in mosaics)**
- **Pattern recognition for ANA, ANCA, AMA, anti-LKM (LKM-like) and mixed patterns based on deep convolutional neural networks, and calculation of titers**
- **Classification of results as positive or negative for Crithidia luciliae, antigen-expressing cells and EUROPLUS antigen dots**
- **Fast processing (13 seconds per image) and consolidation of results per patient for paperless diagnostics**
- **Digital archiving of fluorescence images and reports**
- **Bidirectional data exchange with the laboratory information system (LIS)**

EUROIMMUN Medizinische Labordiagnostika AG

Modern technology from the experts

- Magazine for 500 fields
- Automated slide supply
- DataMatrix code reader
- High-resolution cameras
- Controlled (c)LED for > 50,000 h constant light intensity
- Precise optical system
- Up to 3 different autofocus objectives
- 3D manual control
- RealDrive manual control (optional)
- Oculars (optional)

Paperless generation of result reports in three steps

User-friendly software

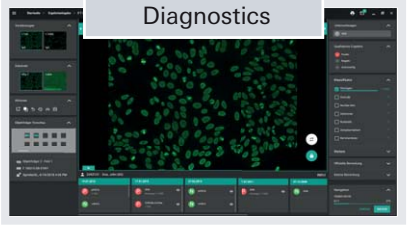
1

After the initiation, the EUROPattern Microscope automatically takes subsequent fluorescence images of all slides. The fluorescence images can be viewed immediately and checked at the screen, while the microscope continues recording the images. The captured images are classified as positive, negative or borderline and the patterns identified, in case of ANA and ANCA, by means of deep learning processes using deep convolutional neural networks.

2

Negative samples are displayed in a clear scroll-down list and can be verified rapidly and reliably all together, taking into account the counterstaining, with a single mouse click. For strongly positive samples the software also suggests individual dilution series for subsequent analyses.

3

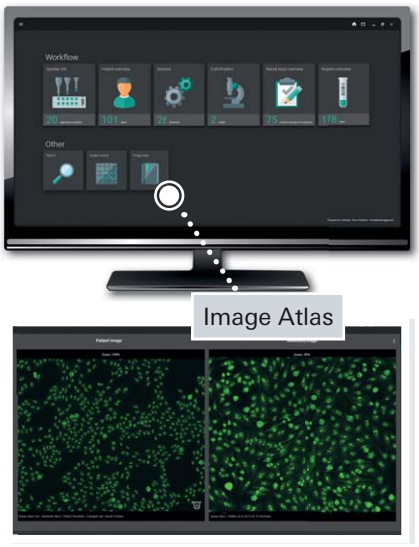


Positive and borderline samples are afterwards displayed for each patient, and all individual results are compiled in an overview. The user can directly confirm the suggested patterns and titers by mouse click, or, if necessary, edit them – the competence remains with the user.

The entire process can be performed completely paperlessly, from the creation of worklists, to diagnostics and archiving of fluorescence images and results. Results from former analyses are shown in a clear patient history.

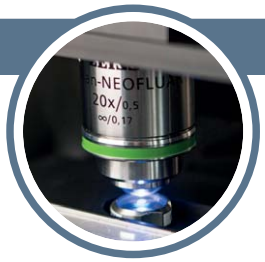
More practice-oriented functionalities

- The intelligent management of all data and results as well as the bi-directional communication with the LIS and the instruments takes place with the laboratory management software EUROLabOffice 4.0.
- Very quick focussing, image recording and digital evaluation (13 seconds/image) allow for the system to be integrated into the workflows of the largest laboratories. Diagnosis suggestions can be already verified during the automated microscopy process.
- With a click of the mouse, the sample field can be automatically approached and manually evaluated in the live mode. In order to prevent fading of the fluorescence, the cLED turns itself off when inactive.
- Automated photographing of tissues for subsequent visual diagnostics at the screen and archiving is also possible.
- By using the EUROLabOffice 4.0 Image Atlas, recorded fluorescence images can be annotated and saved as a reference or for study purposes by one mouse click.



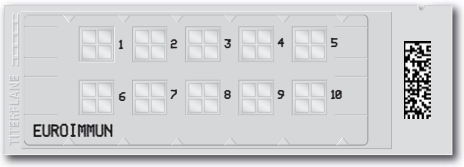
Fluorescence standardisation

- Constant illumination due to the built-in fluorescence standard
- Unique automated calibration of the microscope



Excellent agreement between CAIFM and conventional evaluation

- Allocation of the samples to the corresponding results is ensured through the DataMatrix codes of the slides. The slides can be loaded in any order.



- Focussing in transmitted light prevents the fluorescence from fading.
- The counterstaining enables a reliable quality control of all fluorescence images during diagnostics.
- The controlled EUROIMMUN cLED guarantees standardised excitation light and reproducible fluorescence emissions.
- The integrated fluorescence standard calibrates all EUROPattern microscopes for comparable IIFT images.
- The computer-aided evaluation can be adjusted to the local diagnostic standards with respect to the patterns (e.g. sensitivity).

ANA pattern		Identified pattern (automatic pattern recognition)	
	n	n	%
Homogen.	15	14	93.3
Granular	12	11	91.7
Nucleolar	11	11	100
Centromeres	10	10	100
Nuclear dots	10	9	90
Cytoplasmic	22	22	100
DFS	20	20	100
Nucl. membr.	13	13	100
ANA neg.	79	75	94.9
Total	**192**	**185**	**96.4**

EUROPattern n = 171	Visual evaluation	
	Positive	Negative
Positive	92	4
Negative	0	75
Agreement	97.7%	
κ value	0.95	
Sensitivity	100%	
Specificity	94.9%	
Pos. prediction value	95.8%	
Neg. prediction value	100%	

Computer-assisted IIFT evaluation with deep learning technology

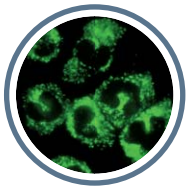
Pattern recognition based on deep convolutional neural networks

The EUROPattern Classifier, which can be integrated into EUROLabOffice 4.0, automatically generates a result proposal (including titer calculation) for a constantly growing number of substrates.
This involves classification of the detected fluorescence patterns by means of deep convolutional neural networks, an artificial intelligence method. All the individual findings obtained with the substrates and dilutions are then consolidated into one result proposal for each patient.

ANA diagnostics

- **HEp-2/HEp-20-10 cells:** Automatically generated pattern and titer proposals with confidence values for nine fluorescence patterns according to the ICAP* (homogeneous, speckled, dense fine-speckled, nucleolar, nuclear dots, centromeres, nuclear membrane, AMA and cytoplasmic) and any combinations thereof

  *ICAP: International Consensus on Antinuclear Antibody (ANA) Patterns
- **Crithidia luciliae:** Automated positive/negative classification and titer proposals based on the specific kinetoplast fluorescence for the detection of anti-dsDNA antibodies

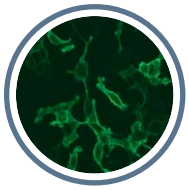


ANCA diagnostics

- **Granulocytes:** Automatically generated pattern and titer proposals with confidence values for the fluorescence patterns pANCA, cANCA and atypical ANCA

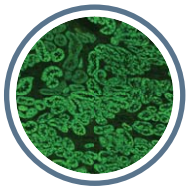
NEW **HEp-2 cells + granulocytes (EOH):** The combination BIOCHIP is used for the targeted differentiation of ANA and cytoplasmic antibodies (result is issued as ANA interference)

- **EUROPLUS antigen dots:** Automated positive/negative classification of the monospecific antigen fluorescence for confirmation and differentiation of specific diseases from the AAV range (GPA and MPA)



Diagnostics based on antigen-expressing cells

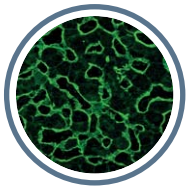
- **Neurology**: Automated positive/negative classification and titer proposal with confidence values for different antigens, e. g. AMPA 1/2, NMDAR, GABAR B1/B2, LGI1, CASPR2, DPPX, aquaporin-4 and MOG
- **Nephrology:** Automated positive/negative classification and titer proposal with confidence values for the antigen PLA2R
- **Infection diagnostics:** Automated positive/negative classification and titer proposal with confidence values for the antigens EBV-CA, EBV-EA and EBNA



Diagnostics of autoimmune liver diseases

- **Liver (rat):** Automated positive/negative classification for relevant ANA and identification of anti-LKM-like patterns (“LKM-like”, is given as “anti-LKM” pattern after a confirmatory result on kidney tissue) to support the diagnosis of autoimmune hepatitis types 1 and 2
- **Kidney (rat):** Automated positive/negative classification for AMA, specific for primary biliary cholangitis, and identification of anti-LKM-like patterns (“LKM-like”, is given as “anti-LKM” pattern after a confirmatory result on liver tissue; suspected autoimmune hepatitis type 2)

NEW **Stomach (rat):** Automated positive/negative classification for ASMA



Diagnostics of autoimmune gluten-sensitive enteropathy (coeliac disease)

NEW **Liver (monkey) IgA:** Automated positive/negative classification for antibodies against endomysium (filamentous linings of the intralobular sinusoids) to support the diagnosis of gluten-sensitive enteropathy

NEW **Oesophagus (monkey) IgA:** Automated positive/negative classification for antibodies against endomysium (lamina muscularis) to support the diagnosis of gluten-sensitive enteropathy