

From BIOCHIPs to artificial intelligence – defining new horizons in IFA

EUROIMMUN has been creating innovative solutions for immunofluorescence diagnostics for over thirty years. CLI talked to *Dr. Panagiotis Grypiotis, Head of Product Management Automation* at EUROIMMUN, to find out about the company's milestones and the newest innovations on the market.

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Why is IFA so important for diagnostics?

The indirect immunofluorescence assay or IFA serves as an essential screening method for detecting many types of antibodies. It offers high sensitivity and specificity, as well as a broad antigen spectrum due to the use of cells and tissues as antigenic substrates.

What are the challenges of IFA?

Manual incubation of the slides requires sufficient staff to perform the assays within the timeframe, where it is always a challenge to find skilled personnel. Traditional microscopic evaluation of the fluorescence patterns is also time-consuming and demands high proficiency from laboratory staff. It is, moreover, based on subjective interpretation by the lab technicians, which can lead to high intra- and inter-laboratory variation. Automated systems can help to solve these problems by improving the efficiency and standardisation of IFA.

How long has EUROIMMUN been active in the field of IFA?

EUROIMMUN has been building expertise in IFA since the 1980's. We possess a broad technology base and extensive know-how, enabling us to design optimal solutions to meet our customers' needs. Having our own production facilities also means that we can react quickly to laboratories' evolving requirements. EUROIMMUN strives to continually propel IFA technology to a new level with cutting-edge solutions for slide processing, microscopy and evaluation.

What was EUROIMMUN's first breakthrough?

One of EUROIMMUN's first pioneering achievements was BIOCHIP Technology, which was invented by the company's founder Professor Dr. Winfried Stoecker in 1983. In this method, miniature sections of different substrates are positioned side by side in the reaction fields of microscope slides and incubated in parallel under standardised conditions using the TITERPLANE Technique. This multiplex approach enables comprehensive antibody profiles to be established with a single analysis. Today, we offer the largest portfolio of IFA substrate combinations on the market encompassing all kinds of diagnostics.

How can the IFA slides be automatically processed?

Today's laboratories have a variety of options for automated processing of IFA slides depending on their sample throughput. Our top-end instrument, the EUROLabWorkstation IFA, was introduced in 2019 and provides fully automated and standardised processing of IFA slides at an unmatched throughput of more

than 200 samples per hour using ten needles. The largest lab chains in the world rely on this speed to manage their very high sample throughput, which reaches into the thousands daily. The system was developed by EUROIMMUN with a focus on data integrity and minimisation of manual processes. Drawing on experience gained from previous milestones, we incorporated our proprietary TITERPLANE incubation and MERGITE! washing technologies to ensure brilliant fluorescence signals. Further instruments such as the IF Sprinter and Sprinter XL are available for smaller sample numbers. These devices are in use in 47 countries all over the world, and the 1000th device has recently been installed at a customer site. As a complementary device for smaller laboratories, EUROIMMUN also developed the tabletop MERGITE! for fully automated slide washing, the only such device on the market. Its controlled liquid flow ensures meticulous washing that is gentle on the substrates, ensuring high-quality results.

When did EUROIMMUN introduce its first specialised microscope?

EUROIMMUN launched its first microscope tailored to indirect immunofluorescence in 2006. The simplified, low-maintenance design incorporated a controlled LED in place of conventional complex illumination fittings. With its long life span, low power consumption and regulated light intensity, the cLED brought a new level of reproducibility, cost-effectiveness and convenience to immunofluorescence microscopy. The cLED technology is now used in our EUROStar III Plus microscope, as well as in our highly successful EUROPattern series.

How did the EUROPattern enhance IFA microscopy?

Computer-aided immunofluorescence microscopy using the EUROPattern system was a landmark development, as it enables complete on-screen evaluation of IFA, thus eliminating the need for a dark room. The EUROPattern Suite, the first version of which was introduced in 2011, consists of a fully automated microscope with slide magazine accompanied by sophisticated software for image recording, pattern interpretation and result archiving. A novel feature is the slide barcode reader to ensure traceability of results. EUROPattern microscopes include precision optics incorporating state-of-the-art Zeiss components to ensure top-quality images. The high-capacity EUROPattern Microscope 1.5 model can process up to 500 fields containing multiple BIOCHIP substrates in one run. It has an image acquisition speed of 13 seconds per image, which established it as the frontrunner in speed. There are currently more than 500 installations of this microscope worldwide.

Tell us about the new EUROPattern Microscope Live

The EUROPattern Microscope Live was launched this year and is a compact model which combines state-of-the-art live microscopy with ultrafast image processing. We consider this microscope to be a game-changer in the field. Our idea was to design a small microscope serving as a standardisation model for small- and medium-throughput laboratories. The end product includes many innovations to enable even faster diagnostics than before. It incorporates novel laser focussing technology, which allows image acquisition in a record 2 seconds per image. It also features an automatic fluorescence calibrator, ensuring standardised light quality between microscopes even at different locations. For live microscopy we included a multi-touch screen on the monitor to allow easy navigation and zooming. The microscope hardware is complemented by the advanced EUROLabOffice 4.0 software, which provides image evaluation incorporating artificial intelligence as well as complete management of analyses and results.

How does the evaluation with AI work?

The software uses deep convolutional neural networks for discrimination of positive and negative results and pattern recognition. For example, in the evaluation of anti-nuclear antibodies (ANA) on HEp-2 cells, which is one of the most commonly performed analyses in autoimmune diagnostics, AI allows us to be a step ahead and include not just nine different patterns, including DFS 70 and AMA, but also combinations thereof to get the most accurate result proposal for every patient. The deep learning algorithms provide effective segmentation of the cells, so that counterstaining is no longer necessary. The software also generates titer suggestions from the fluorescence intensities of the incubated dilutions. The ANA pattern classification is compliant with the International Consensus on ANA Patterns (ICAP), which is an important criterion for our customers. The classifier can also be used to evaluate anti-neutrophil granulocyte cytoplasmic antibodies (ANCA) on granulocyte substrates, anti-dsDNA antibodies on Crithidia luciliae, and autoantibodies associated with autoimmune liver diseases on tissue substrates. We are also currently working on many more applications to add to the repertoire.

What else does the EUROLabOffice 4.0 software offer?

EUROLabOffice 4.0 is an evolution of our established EUROLabOffice middleware and was designed as a laboratory counterpart to Industry 4.0. In line with this, our focus lay on high interconnectivity for maximum data integrity and user convenience. The software serves as a flexible central interface, providing digital laboratory organisation with intelligent networking of workplaces and instruments, for example for IFA, ELISA, chemiluminescence and immunoblot. It can be connected to laboratories' existing information systems, so that data can be exchanged securely and with complete traceability. The software has an intuitive interface, making it easy to use. For instance, the results window displays all findings consolidated into one report per patient, including the patient's history and all images. The system also administers and archives all data, images, results and article information, creating paper-free processes. In a project studying operation efficiency, a diagnostic laboratory was able to increase its throughput from 150 to 250 IFA samples per day by using EUROLabOffice software instead of manual processes, representing an increase in efficiency of 66%. With its versatility and user friendliness, we consider EUROLabOffice 4.0 a significant milestone in the digitisation of the diagnostic laboratory.