Together at the pulse of neurobiology

A unique portfolio of neurobiomarker tests

The testing landscape for neurological diseases has expanded rapidly in recent years due to the characterisation of many novel biomarkers. With over 15 years of experience in neurological analytics, EUROIMMUN offers an unparalleled portfolio of assays for determination of more than 80 neurobiomarkers in autoimmune diseases, neurological infections and Alzheimer's disease. CLI talked to Dr Dominik Jäger, Product Manager for Autoimmune Diagnostics, to find out more.

How is EUROIMMUN involved in neurobiomarker research?

At EUROIMMUN, we are committed to basic research to advance knowledge and build the foundation for developing innovative tests. Our affiliated Institute for Experimental Immunology collaborates with universities, clinics and research institutes worldwide to identify and study novel disease markers, especially in autoimmune neurological diseases. Based on this expertise, we offer one of the largest portfolios of neurobiomarker assays worldwide, including many novel and exclusive parameters.

Tell us about the field of autoimmune neurology

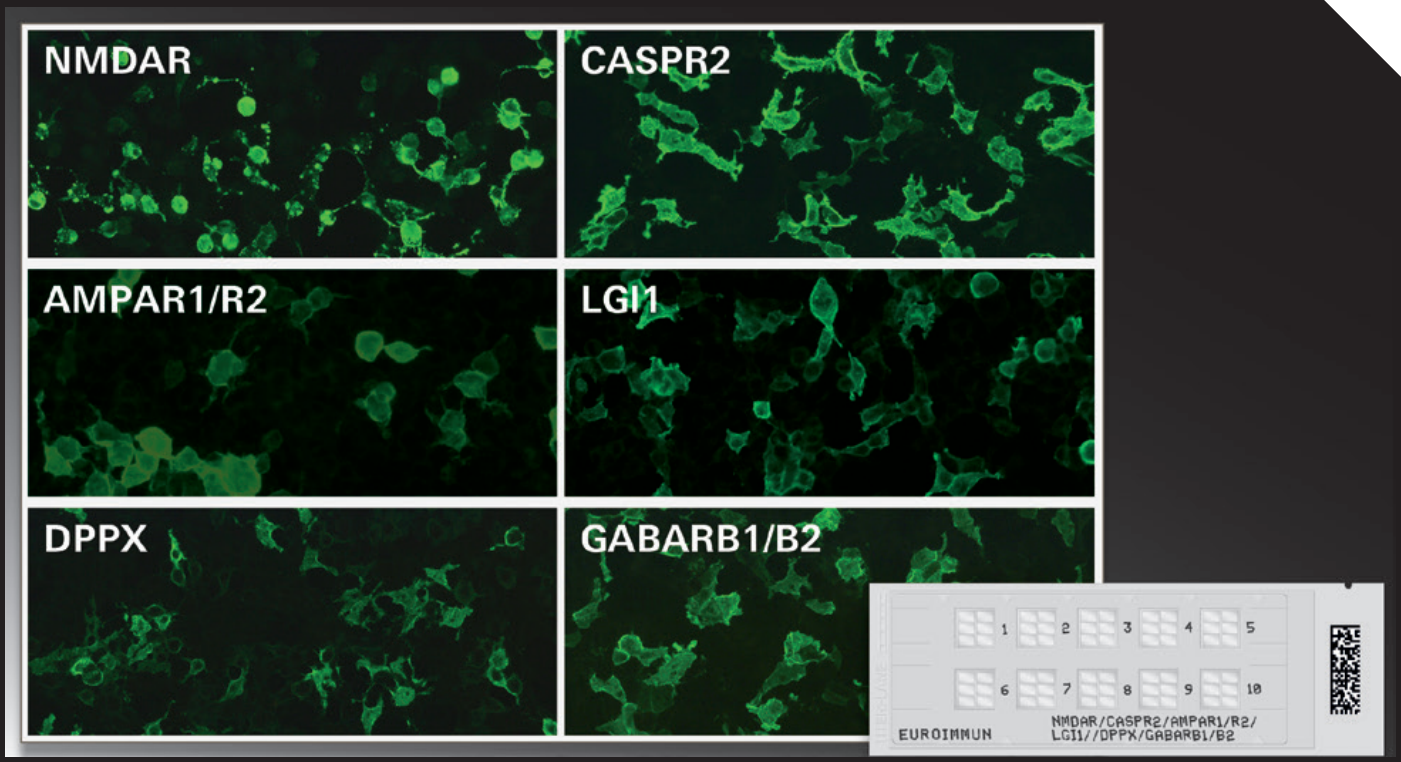
Autoimmune neurology is an incredibly fast-moving field. Just 20 years ago, only a small number of autoantibodies against neuronal targets was known, and these were mostly a phenomenon of cancer and not directly pathogenic. Today, autoimmunity is known to be a direct trigger of brain and nerve inflammation, causing severe deficits in memory, behaviour and movement. An initial breakthrough came in 2007 with the identification of autoantibodies against NMDA receptors in patients with severe psychiatric features. The toll of this autoimmune encephalitis was movingly captured in the bestseller memoir *Brain on Fire: My Month of Madness* by Susannah Cahalan, in which she describes her terrifying descent into psychosis. Nowadays, anti-NMDAR encephalitis can be effectively diagnosed and treated with immunotherapy. A large spectrum of further autoantibodies has since been discovered in autoimmune encephalitis, and new parameters are being added every year. Other types of autoantibodies have been found to be the driving force behind diseases such as autoimmune cerebellar ataxia, demyelinating diseases and autoimmune nodopathies. EUROIMMUN scientists have contributed to this field by identifying as many as 37 new target antigens and co-authoring over 170 peer-reviewed papers.

How are new autoantibodies identified?

Among the most versatile methods for characterizing new autoantibodies is the indirect immunofluorescence assay (IFA). Patient sera that react with neural tissue but not with any known antigens are selected and then analysed by immunoprecipitation and mass spectrometry to identify the antigenic targets. IFA based on transfected cells expressing the target antigen – known as cell-based assays or CBAs – are subsequently used to confirm the new discoveries. This technique has been used by our scientists and research partners to characterize many new autoantibodies. CBAs are especially suitable for expression of fragile, conformation-dependent cell-surface antigens.

How is autoantibody testing used in routine diagnostics?

Autoantibody testing serves as an important diagnostic criterion for various autoimmune neurological diseases. To support clinical labs, we pioneered the first IVDs for key parameters such as anti-NMDAR, anti-AQP4 and anti-IgLON5. Notably, CBAs are now recommended as the gold standard for antibody detection in international guidelines for the diagnosis of anti-NMDAR encephalitis and neuromyelitis optica spectrum disorders. With our renowned BIOCHIP technology, different CBAs and tissue sections can be analysed simultaneously, which can help to increase the overall detection rate since the individual neural autoantibodies are in many cases quite rare. Immunoblots are another important method in neurological diagnostics, allowing multiparameter detection of autoantibodies against more stable intracellular antigens, for example in paraneoplastic neurological syndromes. Our EUROLINE tests enable detection of autoantibodies against up to 12 antigens in parallel and are among the most comprehensive on the market. Our assays are all fully automatable, which is an important aspect for today's time-stressed laboratories.



What tests does EUROIMMUN offer for CNS infections?

We offer a range of ELISAs for detection of pathogen-specific antibodies in the cerebrospinal fluid (CSF). This is an important investigation in the diagnosis of acute or chronic inflammation of the central nervous system (CNS), which can be caused by infections with various viruses, bacteria or parasites or by polyclonal stimulation in diseases such as multiple sclerosis. We have recently introduced our CSF ELISA 2.0 series of assays, which have been optimised to improve handling and save resources. A special feature of the tests is the option to store a master calibration curve, which increases cost-effectiveness by eliminating the need to incubate calibrators each time. We have also developed specialised software that performs the complex computation of the antibody indices, saving a lot of time and effort for our customers. Additionally, we have developed the first CE-marked ELISA to determine CXCL13 in CSF as an early indicator of Lyme neuroborreliosis.

What about Alzheimer's disease?

The advent of new disease-modifying drugs for Alzheimer's disease is an exciting development that promises to slow progression of the disease in some individuals. But these drugs need to be applied in the early phase of mild cognitive impairment, requiring timely and accurate diagnosis. The most important diagnostic biomarkers for early diagnosis of Alzheimer's disease are beta-amyloid 1–42 to 1–40 ratio, total tau and P-tau measured in CSF. CSF is currently recommended over blood as it enables more sensitive analysis. Of note, CSF beta-amyloid is the earliest known marker of Alzheimer's pathology and can often be detected years before symptoms start. We have developed ELISAs and ChLIAs which provide precise measurement of these proteins in patient CSF samples.

Our scientists were also part of a consortium that created the first official guideline for preanalytical sample handling to help laboratories maximise the reliability of their results.

What does *APOE* genetic testing offer?

APOE genotyping is increasingly recommended as a screening test prior to applying anti-amyloid therapies in Alzheimer's disease patients. This is because carriers of the *APOE* ε4 allele, especially homozygous carriers, have a higher risk of adverse effects from these drugs. We are developing a real-time PCR assay that detects the three alleles ε2, ε3 and ε4 and determines the genotype. The test will be launched soon, and we hope it will help support therapy management using a more patient-centred approach.

Where can readers find out more?

We have established a dedicated web portal for neurology bringing together our research publications and product information into one central place. This can be found at *www.neuro-company.com*.

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