The new test generation for Alzheimer’s disease diagnostics

EUROIMMUN Beta-Amyloid (1-40) ELISA
EUROIMMUN Beta-Amyloid (1-42) ELISA
EUROIMMUN Total-Tau ELISA

- No matrix effect – excellent reproducibility
- Lyophilised calibrators – for convenience and precision
- Improved diagnostics through ratio calculation
- Standardised protocols
- Automatable – personnel and time savings
- CE certification – optimal for accredited laboratories
Alzheimer’s disease

A global challenge

According to estimations of the WHO, Alzheimer’s disease is the most frequent neurodegenerative disease in the world. Recent figures show that there are approximately 36 million cases of Alzheimer’s disease worldwide. This figure will probably double by 2030. Patients who first attend a neurologist usually present with learning difficulties and short-term memory impairment. During the course of the disease, cognitive deficits increase further, leading to the so-called mild cognitive impairment (MCI) stage. In the final stage of the disease, the patient is unable to go to work or to manage everyday life. From this stage on, the remaining life expectancy is on average seven to ten years.

Pathological characteristics, clinical diagnosis and imaging techniques

Alzheimer’s disease manifests itself by the formation of deposits in the cell body and outside the nerve cell ends. The intracellular deposits consist of proteins that are important for the cell structure. These so-called tau proteins accumulate a higher quantity of phosphates, thus forming tangled fibre strands (phosphorylated tau/P-tau). The extracellular deposits (plaques) result from elimination products of a precursor protein located in the membrane (amyloid precursor protein). The physiological function of the eliminated peptides Aβ 1–40 and Aβ 1–42 has not yet been fully understood. But it is assumed that they play a major role in the signal transmission of nerve cells.

Definitive diagnosis of Alzheimer’s disease can only be established post mortem. The neuropathological changes (plaques and tau fibre strands) in the brain of patients with Alzheimer’s disease are only visible during autopsy. Accordingly, the tentative diagnosis of Alzheimer’s disease is based primarily on the clinical sign of memory loss ("probable Alzheimer’s disease"). Imaging techniques such as MRT, SPECT or PET (amyloid detection) can be used to support early and differential diagnostics (e.g. exclusion of endocrinopathies and electrolyte disorders). The results from imaging dementia diagnostics are then assessed together with other available diagnostic information. This also includes CSF-based analyses.

Alzheimer’s disease diagnostics using ELISA

The diagnosis of Alzheimer’s disease in early and presymptomatic stages requires quantifiable and reliable biomarkers. CSF samples from patients with Alzheimer’s disease show, for instance, significantly decreased Aβ 1–42 concentrations and increased total-tau levels. CSF analysis is performed using the EUROIMMUN Beta-Amyloid (1-40), Beta-Amyloid (1-42) and Total-Tau ELISAs.

The Aβ peptides and tau protein are each bound by a capture antibody and then detected by a secondary antibody. Due to interchangeable reagents and identical protocols the analysis can be carried out in four hours. Lyophilised calibrators and controls ensure convenient test performance, high precision and clinical accuracy. Both ELISAs are CE labelled and automatable, allowing CSF diagnostics to be easily integrated into the automated routine operations of a diagnostic laboratory.

Neuron showing pathological characteristics of Alzheimer’s disease

Epitopes of beta-amyloid and tau antibodies
The EUROIMMUN Beta-Amyloid (1–42) ELISA allows matrix-independent detection. Whereas the measurement values obtained with tests from other suppliers varied considerably, the measurements yielded by the EUROIMMUN ELISA remained virtually constant.

**Improved early and differential diagnostics using ratio calculation**

The calculation of the ratio of Aβ 1–42 and Aβ 1–40 can help to increase the efficiency of early diagnostics. Aβ 1–40 is a measure of the individual amyloid expression and is not changed in Alzheimer’s disease. The case study shows the CSF sample from a patient with a high basal expression of beta amyloids. By evaluating only Aβ 1–42, the patient cannot be clearly classified. With the calculation of the ratio, however, the patient can be definitely diagnosed.

The above figure shows that the calculation of the amyloid ratio is also helpful in the difficult clinical differentiation of Alzheimer’s disease from vascular dementia.
Automation of EUROIMMUN ELISAs for Alzheimer’s disease diagnostics

Automatable for all parameters

EUROIMMUN ELISAs for the determination of beta-amyloid (1–40), beta-amyloid (1–42) and total tau can be processed reliably and quickly using the EUROIMMUN Analyzer I or I-2P. These automated systems identify samples and reagents easily by means of barcodes, thus preventing mix-ups. The target values for controls and calibrators are no longer entered individually, but are registered automatically. After loading, the processing is fully automated right up to completion of the analyses (“walk-away function”). The results are then sent directly to the laboratory computer. Detailed validation documents are available for all test systems.

Direct comparison between manual performance and automated analysis of the Beta-Amyloid (1–40), Beta-Amyloid (1–42) and Total-Tau ELISAs using the EUROIMMUN Analyzer I shows a very high agreement of results. The coefficient of correlation, which measures the degree to which two variables are linearly related, is 0.970. This represents an agreement of almost 100%.

ADx Neurosciences – a strong partner

The Beta-Amyloid (1–40), Beta-Amyloid (1–42) and Total-Tau ELISAs from EUROIMMUN were developed in collaboration with ADx Neuro-sciences. During the past 20 years, the founders of ADx Neurosciences have been the driving force behind the development, market launch and commercialisation of the most-used CSF biomarker assays for the diagnosis of Alzheimer’s disease.

Product overview

<table>
<thead>
<tr>
<th>ELISA</th>
<th>Order no.</th>
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<tbody>
<tr>
<td>Beta-amyloid (1–40)</td>
<td>EQ 6511-9601-L</td>
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<tr>
<td>Beta-amyloid (1–42)</td>
<td>EQ 6521-9601-L</td>
</tr>
<tr>
<td>Total tau</td>
<td>EQ 6531-9601-L</td>
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Manual measurement (pg/ml) vs. Automated measurement (pg/ml)