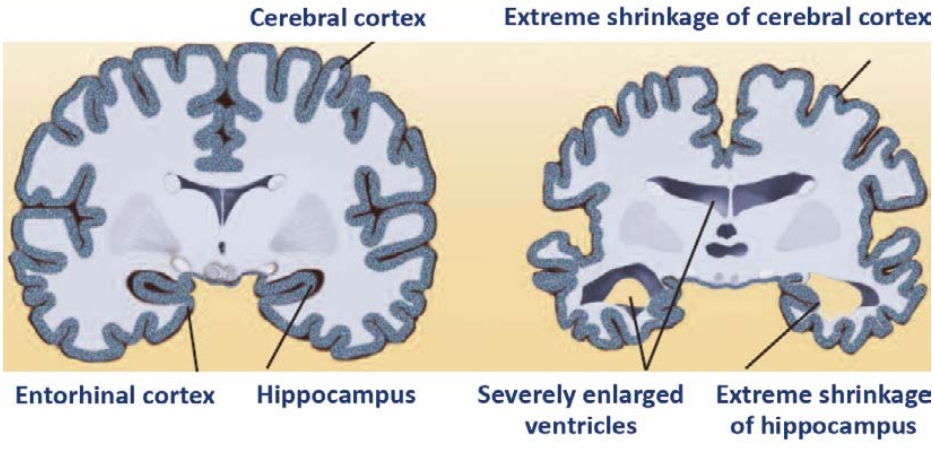
Providing diagnostic solutions for Alzheimer's disease

IBL International, the latest addition to the Tecan Group, offers a range of microplate-based immunoassays to help diagnose Alzheimer's disease, a devastating condition that significantly impacts the lives of both sufferers and their families. Early diagnosis is essential for implementation of appropriate treatment and support mechanisms, enabling patients to live as independently as possible.

Alzheimer's disease (AD) is the most commonly encountered form of dementia, affecting not only the elderly but, in some cases, much younger people. IBL International has been marketing assays for research purposes for more than 15 years and, since early 2014, has offered an *in vitro* diagnostic (IVD) assay for amyloid-beta (Aβ) 1-42* – a known biomarker of Alzheimer's – as well as the reference protein Aβ 1-40. International Product Manager Oliver Schmidt discussed the pathology of the disease and the Company's diagnostic solutions: "Alzheimer's disease is characterized by cognitive impairment, but it is only during post-mortem examination of the brain that the hallmark protein deposits – amyloid plaques and tau fibrils – and brain shrinkage can be definitively identified. However, AD will have begun to take hold many years earlier, long before cognitive deficiencies were visible, and this is one of the main limitations in developing therapeutics for Alzheimer's. Biomarker analysis has the potential to change this situation. We know that amyloid plaques are a characteristic of AD, and that the precursor amyloid-beta proteins that form these deposits are present in the cerebrospinal fluid (CSF); measurement of these precursor proteins therefore provides an indication of a patient's disease status."

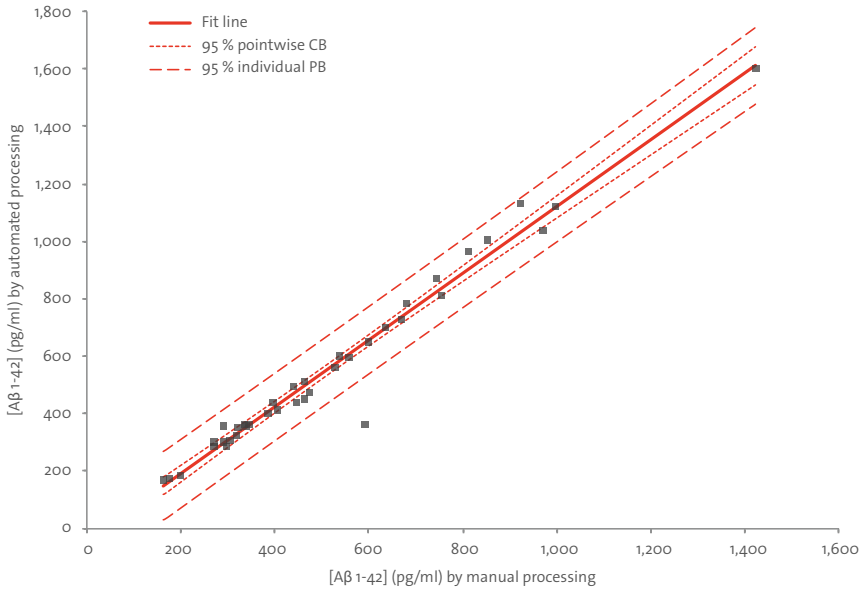
Oliver continued: "Formed by enzyme-mediated cleavage of the amyloid-beta precursor protein (APP), amyloid-beta peptides can exist in several isoforms, but the one that is pathologically important in Alzheimer's disease is Aβ 1-42. This is the main constituent of the brain plaques, and AD patients typically have a lower than usual concentration of Aβ 1-42 as the protein oligomerizes to form plaques, with a corresponding decrease in monomer concentration. Although Aβ 1-42 is the main isoform, this alone does not give a complete picture, and the total level of Aβ should be studied to account for people who are naturally low or high Aβ 1-42 producers. This could give rise to a false positive diagnosis and so, to prevent this happening, the Aβ 1-42 result is normalized to the level of Aβ 1-40. Because Aβ 1-40 is consistently around 60 % of the total Aβ produced, this presents a clearer picture, and clinical studies have shown the superiority of using the Aβ 1-42 to Aβ 1-40 ratio rather than measurement of Aβ 1-42 alone."



Generally, subjective clinical measures such as the 'clock drawing' and 'three-word delay' exercises are used for the initial assessment of cognitive impairment, supported by the analysis of biomarkers – such as amyloid and tau – using immunoassays, helping to confirm the diagnosis. "We already had good manual amyloid-beta assays for research purposes, and optimized these for IVD use* with CSF," said Oliver. "These assays offer several advantages. Low variance is essential, and our kits typically have CVs of far less than 10 %, comparing well with other available assays. Another benefit is that they are sensitive enough to allow predilution of the sample. The amyloid assays, for example, include a 1:20 predilution step, eliminating matrix effects and enabling amyloid-beta measurement in the low picomolar range, as well as allowing both Aβ biomarkers to be determined in a single dilution of a small volume of CSF. Assay times are also short, enabling results to be generated in just three and a half hours. The Aβ assays have now been adapted for fully automated processing

on the Freedom EVOlyzer®, and we are also in the process of implementing a tau assay on this platform. With automation, we simply prepare the workdeck, program the workstation and start the assay. The reproducibility is excellent."

IBL assays have already been implemented at MVZ Volkmann in Karlsruhe, Germany. Chemist Oliver Bauer, who is responsible for technical validation of the laboratory's results, explained: "We process about 150 samples a month for each of the AD biomarkers. At present, we use the Aβ 1-42 ELISA for routine testing – the kit includes three sets of standards and controls, which is a perfect match for our schedule of two runs a week – and, now that the evaluation is complete, will be implementing the Aβ 1-40 assay in early 2015. We chose IBL assays for their wide linear range and good reproducibility, due to low inter-lot variation.



Comparison of results obtained manually with automated processing on the Freedom EVOlyzer

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The kit design is another benefit; ready to use standards and controls, plus matched protocols and reagents for the different biomarker assays, make it easier to process the ELISAs. We really appreciate the effort IBL puts into developing products to meet its customers' requirements."

To find out more about IBL International, visit **www.ibl-international.com/en**

To find out more about MVZ Volkmann, visit **www.laborvolkmann.de/analysenspektrum/HTML/index.html**

*CE-IVD marked for Europe, not available for clinical use in USA.