
NEURODEGENERATION
RESEARCH.
TECAN.

# THE HALLMARKS OF NEURODEGENERATION.

**Discover Tecan's broad range of solutions optimized for neurodegeneration biomarkers measurement, designed to keep your research at the forefront of the latest trends in the field.**

Neurodegeneration or neurodegenerative diseases are a group of disorders that are characterized by progressive loss of structure respective function of neurons, including their death.

Most known neurodegenerative diseases are Alzheimer's disease, Parkinson's disease, Multiple sclerosis and Amyotrophic Lateral Sclerosis. Yet, research in the field of neurodegeneration elucidates many more often overlapping diseases that have similar cellular and sub-cellular pathogenic mechanisms.

Usually the neurodegenerative diseases can be characterized by specific patterns of misfolded proteins as shown in the **figure 1**. As a consequence research is focusing on measuring these proteins in the different body fluids.

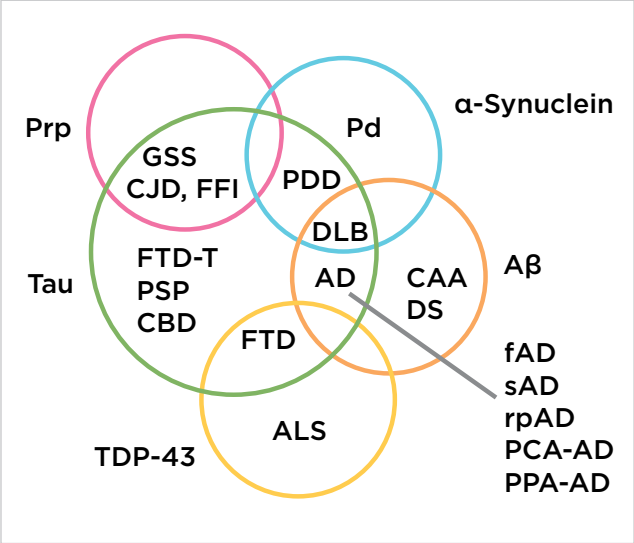



**Figure 1**: Involvement of different prion-like proteins in multiple neurodegenerative disorders. The figure depicts the overlapping pathological profile of Prion Protein (PrP, pink circle), α-Synuclein (blue circle), Amyloid-β (Aβ, orange circle), Tau (green circle), and TDP43 (yellow circle). Each of the stated disorders have further clinical variants (as shown in the case of AD), thereby complicating the role of prion-like proteins in bringing about the observed pathology. PDD: Parkinson's disease with dementia; DS: Down's syndrome; FTD-T: frontotemporal dementia with tau pathology; fAD—familial AD; sAD—sporadic AD; rpAD—rapidly-progressive AD; PCA-AD—posterior cortical atrophy–AD; PPA-AD—primary progressive aphasia with AD.1

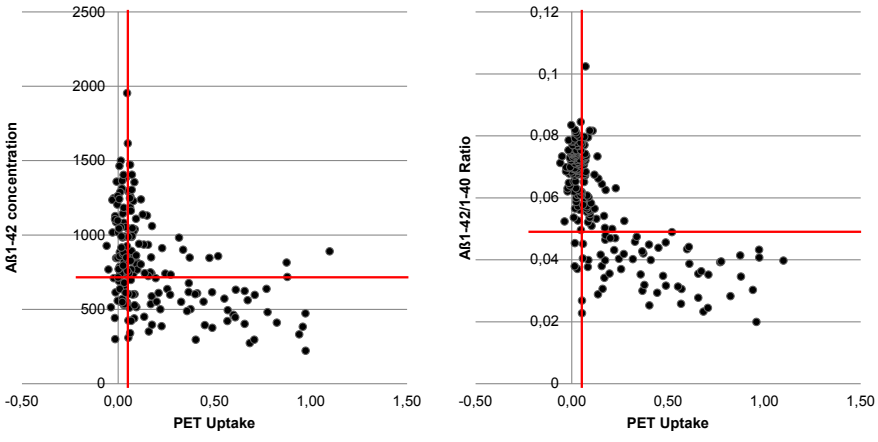



**Figure 2** The Amyloid-beta ratio of Amyloid-beta (1-42) to Amyloid-beta (1-40) significantly improves the accuracy of concordant samples in comparison to PiB from 74.9% to 89.4% [2]

## AMYLOID-BETA AND TAU

Alzheimer's disease (AD), a neurodegenerative disease leading to dementia, can be characterized by 3 hallmarks, which are formation of Amyloid-beta plaques, TAU fibrils and loss of neurons and synapses, leading to a significant brain volume reduction. The first 2 hallmarks lead to the fact that measuring these proteins in CSF is a valuable tool to support the research of Alzheimer's disease.

To assess Amyloid-beta pathology in AD more recent clinical research has shown that the determination of the

Amyloid-beta ratio of Amyloid-beta (1-42)/Amyloid-beta (1-40) significantly improves the understanding of amyloid-beta pathology (Figure 2). Furthermore, as fibril formation of TAU proteins is characterized by hyperphosphorylation, the determination of either phosphoTAU or the non-phosphorylated TAU fraction (Non-pTau) might help to confirm the TAU pathology in AD.

| Parameter | Cat. No. | Method | Reg. Status |
|---|---|---|---|
| Amyloid-beta (1-40) CSF | RE59651 | ELISA | RUO* |
| Amyloid-beta (1-42) CSF | RE59661 | ELISA | RUO* |
| PhosphoTAU** | 30218778 | ELISA | RUO* |
| hTAU total** | 30218780 | ELISA | RUO* |
| Non-pTAU** | RE59641 | ELISA | RUO* |
| p231 TAU** | 30227873 | ELISA | RUO* |
| TAU AGGREGATE** | 30227874 | ELISA | RUO* |

## NEUROFILAMENT-LIGHT

Neurofilaments are the backbone of the neuronal cytoskeleton. Neurofilament light is found to be elevated in neurodegenerative disorders that are associated with the destruction of white matter (substantia alba). Typically these are:

- Parkinson's disease (PD)
- Multiple Sclerosis (MS)
- Amyotrophic Lateral Sclerosis (ALS)

| Parameter | Cat. No. | Method | Reg. Status |
|---|---|---|---|
| Neurofilament-Light (NF-Light) CSF** | 30112458 | ELISA | RUO* |
| Neurofilament-Light (NF-Light) Serum** | 30210101 | ELISA | RUO* |

## PRION PROTEINS

Several human degenerative diseases appear as a result of misfolding and aggregation of proteins. The prototype central nervous system proteinopathy is CJD, in which neuronal prion protein (PrP) with high α-helical content switches into a stable structure rich in β-pleated sheets in a self-catalyzing process that eventually causes a plethora of neurological and psychiatric symptoms.

The identification of this disease, which is extremely serious for the patient, and which shot to prominence in the bovine spongiform encephalopathy crisis, by distinguishing it from forms of dementia such as AD is a major challenge in neurochemical diagnostics. This is because atypical AD phenotypes can be presented with high levels of total Tau protein and/ or positive 14-3-3 protein in the CSF, reflecting intense neuronal degeneration similar to what is found in CJD. The current diagnostic criterion is unfortunately characterized by a diagnostic specificity of 71 % for CJD. Ideally, an additional biomarker more closely related to the pathological process would be helpful in these cases.

| Parameter | Cat. No. | Method | Reg. Status |
|---|---|---|---|
| BetaPrion® Human** | 30227871 | ELISA | RUO* |

Recent studies have shown that atypical cases of AD can be clearly distinguished from CJD via the detection of Prion protein in CSF samples[3]. The BetaPrion® human ELISA precisely enables quantification of this biomarker and may be beneficial in addition to the current classic biomarkers.

## A-SYNUCLEIN

α-Synuclein is an abundant neuronal 140 amino acid protein, predominantly localized in the presynaptic terminals, and involved in vesicle fusion and neurotransmitter release. Aggregates of α-Synuclein are the main components of Lewy bodies (LB), which are intracellular inclusions characteristic for certain neurodegenerative diseases referred to as α-synucleinopathies. These include Parkinson's

disease (PD), Parkinson's disease dementia (PDD), dementia with Lewy bodies (DLB) and multiple system atrophy (MSA).

However, α-Synuclein aggregates are also found in approximately half of sporadic AD pathologies; consequently, it is crucial to differentiate it from pure AD forms. Via the hSYN total ELISA, Tecan offers an improved ELISA, provided by Roboscreen, for detection of total human α-Synuclein. Additionally, the discrimination of total α-Synuclein and disease-specific α-Synuclein is of special interest for distinguishing between different patient groups.

| Parameter | Cat. No. | Method | Reg. Status |
|---|---|---|---|
| hSYN total** | 30227869 | ELISA | RUO* |
| α-Synuclein PATHO** | 30227870 | ELISA | RUO* |

The Anti-human α-Synuclein 5G4, monoclonal antibody strongly binds to the high molecular weight fraction of β-sheet rich oligomers, while no binding to primarily disordered oligomers or monomers is observed. This outstanding capability is used for the human α-Synuclein PATHO ELISA suggesting a promising tool for PD.

### TDP43

The transactive response region DNA-binding protein 43 (TDP43) binds both DNA and RNA and is involved in transcription and splicing. Under pathophysiological conditions, TDP43 accumulates in the cytoplasm and is hyperphosphorylated and/ or ubiquitinated, and this is characteristic for the cytoplasmic inclusions observed in ALS and in many cases of frontotemporal lobar degeneration syndrome (FTLD). Furthermore, TDP43 pathology is also detected in 20-50 % of AD patients and appears to be associated with greater brain atrophy, memory loss, and cognitive impairment. Several studies have been reported on CSF and plasma TDP43 in the context of ALS and FTLD, but research has been hindered by difficulties with detecting the protein. Overall, research suggests that blood based TDP43 may have a role in neurodegenerative biomarkers and could be more useful than CSF TDP43.

| Parameter | Cat. No. | Method | Reg. Status |
|---|---|---|---|
| hTDP43 total** | 30227872 | ELISA | RUO* |

## MEASURING NEURONAL BIOMARKERS IN BLOOD.

As CSF has disadvantages in sampling and not all patients do receive a lumbar puncture (e.g. PD, LBD... patients) studies have shown the usefulness of measuring certain biomarkers also in blood.

### BOOST YOUR BLOOD PLASMA DATA.

Easily eliminate inhibiting matrix effects and enrich your target by immunoprecipitation using TECAN's NEURO IP product portfolio provided by Roboscreen for total TAU, p50Tau, brain-derived TAU, beta-Amyloid, and patho-oligomeric alpha-Synuclein, enhancing the performance of your downstream assay of choice. The downstream analysis can then be any type of assay system, such as the Roche Elecsys®, the Mesoscale QuickPlex, Quanterix SIMOA®, Fujirebio Lumipulse® or even any type of ELISA.

| Parameter | Det. | Cat. No. | Method | Reg. Status |
|---|---|---|---|---|
| Neuro-IP Kit** | 24 | 30251462 | IP Kit | RUO* |
| Brain-derived TAU** | 6 IP | 30251464 | Immuno Beads | RUO* |
| Brain-derived TAU** | 24 IP | 30251465 | Immuno Beads | RUO* |
| Total TAU** | 6 IP | 30251466 | Immuno Beads | RUO* |
| Total TAU** | 24 IP | 30251467 | Immuno Beads | RUO* |
| Human beta-Amyloid** | 6 IP | 30251468 | Immuno Beads | RUO* |
| Human beta-Amyloid** | 24 IP | 30251469 | Immuno Beads | RUO* |
| p50-TAU** | 6 IP | 30251470 | Immuno Beads | RUO* |
| p50-TAU** | 24 IP | 30251471 | Immuno Beads | RUO* |
| Patho-oligomeric α-Synuclein** | 6 IP | 30251472 | Immuno Beads | RUO* |
| Patho-oligomeric α-Synuclein** | 24 IP | 30251473 | Immuno Beads | RUO* |

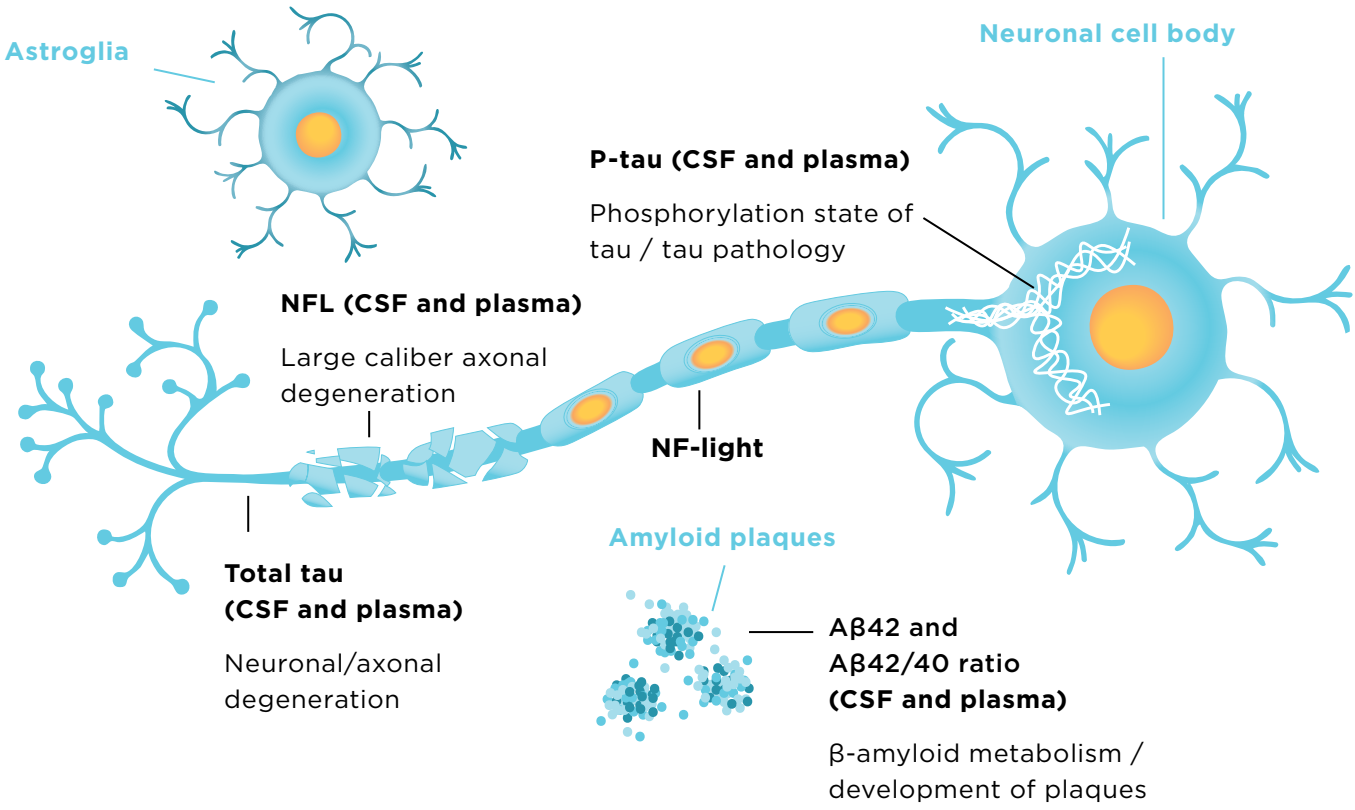
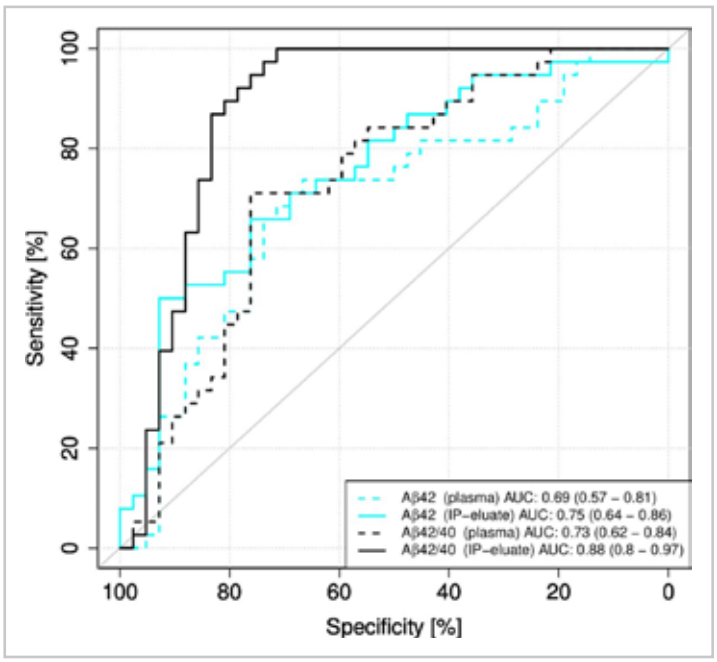



**Figure 3**: Overview of different biomarkers for neurodegenerative diseases and respective sample types, where they have been measured already. Adapted from O. Hansson.[4]




## ELECSYS®

The inclusion of pre-analytical immunoprecipitation in the plasma amyloid-β (Aβ) 42/40 ratio assay significantly improved the accuracy in identifying subjects with abnormal cerebrospinal fluid (CSF) Aβ42/40 ratios. In particular, the area under the receiver operating characteristic (ROC) curve (AUC) increased from 0.73 to 0.88 (p = 0.01547) when IP was applied, demonstrating a significant improvement in performance. A similar improvement was observed when a biomarker-supported clinical diagnosis was used as a secondary endpoint, with the AUC rising from 0.77 to 0.92 (p = 0.01576).[5] This data strongly supports the use of immunoprecipitation in plasma-based assays for Alzheimer's disease as a means to improve accuracy in detecting amyloid biomarkers, potentially facilitating early detection and better cohort selection for clinical trials.

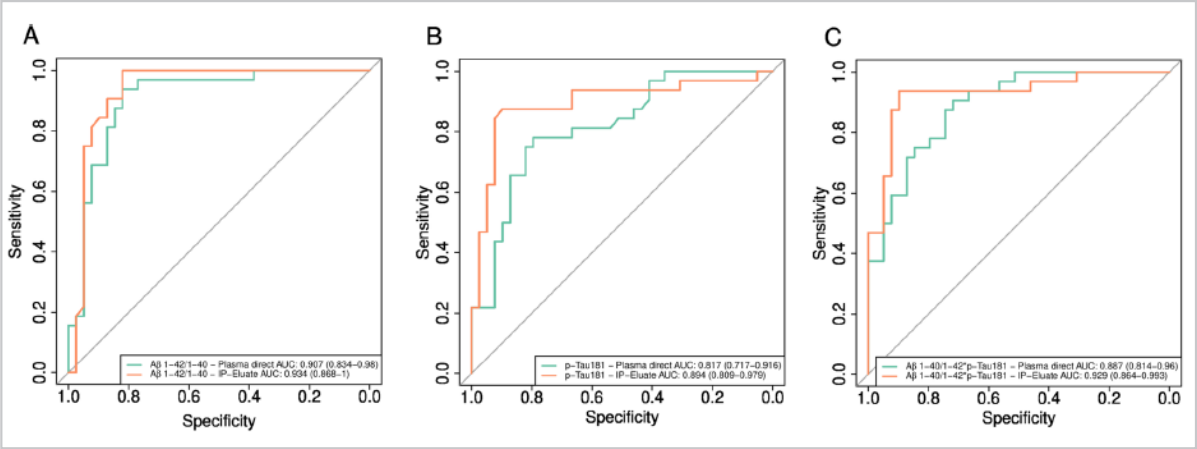
## LUMIPULSE®

Immunoprecipitation of amyloid-beta (Aβ) and phosphorylated Tau (pTau) significantly improved the accuracy of these biomarkers in plasma samples.

Pre-analytical Aβ immunoprecipitation (IP) led to a statistically significant increase in the standardized effect size (Cohen's d), from 1.62 to 2.03 (p = 0.033), improving the differentiation between amyloid-positive and amyloid-negative individuals.

concentrating the biomarkers. This reduction led to better contrast, as demonstrated by the improved AUCs for both Aβ and pTau assays.

Enhanced Specificity and Sensitivity: The pre-analytical treatment allowed for improved classification of individuals with changed amyloid condition, achieving higher sensitivity and specificity in detecting Alzheimer's biomarkers. The combined use of Aβ1-42/1-40 ratios and pTau181 after IP




For phosphorylated Tau 181 (pTau181), pre-analytical Tau-IP increased the accuracy. The area under the receiver operating characteristic (ROC) curve (AUC) increased from 0.817 to 0.894 (p = 0.039), and the effect size (Cohen's d) improved from −1.17 to −1.48 (p < 0.001).

Matrix Effect Reduction: Pre-analytical IP was primarily aimed at reducing matrix effects rather than

showed a marked increase in differential performance compared to direct plasma measurements.[6]

Overall, pre-analytical immunoprecipitation significantly enhances the value of blood-based biomarkers for Alzheimer's disease, supporting its integration into laboratory workflows.

## MESOSCALE

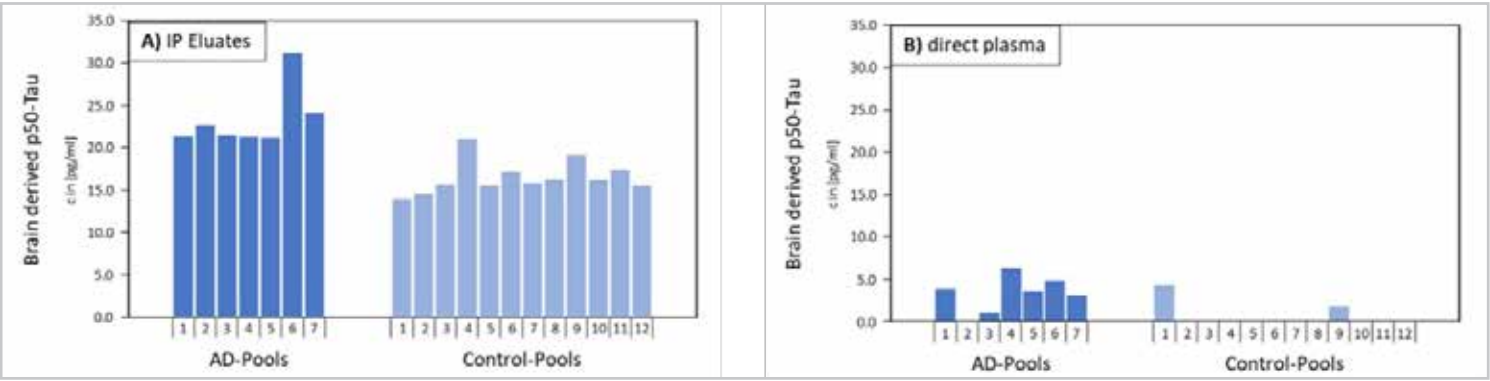
Immunoprecipitation (IP) played a critical role in the study by Klafki et al.[7] for improving the detection of Alzheimer's disease biomarkers. Specifically, the use of IP enabled the selective pre-concentration of amyloid-beta (Aβ) peptides from blood plasma, which greatly enhanced the sensitivity of the subsequent immunoassay. The two-step immunoassay, which included a magnetic bead-based IP followed by chemiluminescent detection, was developed to

measure Aβ−3–40 (APP669–711), a variant of the amyloid precursor protein.

In conclusion, IP was a critical step for improving the sensitivity, specificity, and repeatability of Aβ peptide detection in the study, providing a strong foundation for the development of assays aimed at detecting Alzheimer's disease biomarkers.

## SIMOA®

In an in-house study conducted by Roboscreen, pre-analytical Tau immunoprecipitation (IP) from blood samples enabled clear differentiation between Alzheimer's disease (AD) and control pools using a self-developed SIMOA assay for threonine-50 phosphorylated, brain-derived TAU (p50-DB-Tau). In contrast, direct measurement without Neuro-IP could only detect 8 out of 19 plasma samples, with overlapping results between the AD and control pools.

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IBL International GmbH
Flughafenstrasse 52a
22335 Hamburg
Germany

Phone: +49 (0)40-53 28 91-0
Fax: +49 (0)40-53 28 91-11
Email: IBL@Tecan.com
www.tecan.com/ibl

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