

# Biomarker Profiling for Neurodegenerative Diseases

## ELISAs, Antibodies & Proteins



### **Pre-analytical enrichment of AD biomarkers from plasma by immunoprecipitation**

- Enrichment of the AD relevant proteins total Tau, p50-Tau, brain-derived Tau, beta-Amyloid
- Combinable with a detection system of choice

### **Easy-to-handle and ultra-sensitive immunoassays**

- Proven reliability by certification or relevant clinical studies
- Enabling categorization of different neurodegenerative diseases

### **Unique proteins & antibodies**

- Fast and easy implementation: comprehensive recommendations for use
- Flexible and broad application: suitable for ELISA, Western blot, immunohistochemistry and flow cytometry



## Pre-analytical Enrichment of AD biomarkers from plasma

The increasing number of AD cases worldwide calls for advancing the low-invasive and low-cost plasma analysis of AD pathology biomarkers. But these biomarkers are only found in small amounts in plasma, making them difficult to measure. The Neuro IP Kit enables the enrichment of AD relevant proteins such as total Tau, the brand-new markers p50-Tau and brain-derived Tau as well as beta-Amyloid (A $\beta$ ) from plasma by immunoprecipitation. As a positive side effect, all non-specific matrix effects that

can interfere with downstream analysis are eliminated. The analysis of the enriched AD biomarkers can be performed with a detection system of choice (SIMOA, Lumipulse, MSD, ELISA).

Combine our Neuro IP Kit with mAb coupled immuno beads for enrichment of the target of your choice: total Tau, p50-Tau, brain-derived Tau and beta-Amyloid. We can also provide automation solutions for the Neuro IP Kit – Contact us to find the optimal application solution for you.

## Tau protein and beta-Amyloid

Tau is a microtubule-associated protein that occurs in six human isoforms predominantly located in the axons of neurons. Neuronal and/or glial inclusions of Tau can be detected in several neurodegenerative diseases, or "tauopathies", including the prominent Alzheimer's disease (AD), which may be characterized by their Tau isoform profile. The neurofibrillary tangles (NFT) characteristic for AD are composed primarily of hyper-phosphorylated Tau. In cerebrospinal fluid (CSF), decrease of beta-Amyloid 1-42 (A $\beta$ 42) and a low ratio of A $\beta$ 42 to beta-Amyloid 1-40 (A $\beta$ 42/A $\beta$ 40), together with an increase of both total Tau protein (t-Tau) and phosphorylated Tau (p-Tau), contribute to the "Alzheimer's signature". However, increased Tau levels are found in other neurodegenerative diseases as well. These disorders include, inter alia, frontotemporal lobar degeneration (FTLD), Pick's disease, and corticobasal degeneration (CBD). In Creutzfeldt-Jakob disease (CJD), CSF t-Tau levels are very high, whereas p-Tau is close

to normal, enabling no discrimination between AD and CJD. Several studies showed non-phosphorylated Tau protein (non-pTau) to be a potential biomarker for early detection of AD [1]. Furthermore, non-pTau has been described to be a valuable tool for discrimination of AD from CJD [2].

The hTAU total ELISA detects all isoforms of Tau protein and estimates total Tau content. Additionally, the phosphoTAU ELISA identifies phosphorylated Tau proteins. The non-pTAU ELISA utilizes a monoclonal antibody specific to the non-phosphorylated TPP sequences of the Tau protein (positions T175 and T181). The portfolio is rounded out by the novel p231TAU ELISA.

Unique monoclonal antibodies against all isoforms of Tau protein, phosphorylation, double-phosphorylation, and splicing forms as well as antibodies recognizing deposits of beta-Amyloid 1-42 in brains of Alzheimer's disease patients and transgenic mouse models are also available.

[1] Lewczuk et al. (2017) J. Alzheimers Dis. doi: 10.3233/JAD-160448

[2] Ermann et al. (2018) Ann. Clin. Transl. Neurol. doi: 10.1002/acn3.584



# Order Information

## Pre-analytical Enrichment of AD biomarkers from plasma **NEW**

Order number	Description
[x] = [1]: 6x IP, [2]: 24x IP	
847-0108000108	Neuro IP Kit
847-060100010[x]	Immuno Beads total Tau
847-060100020[x]	Immuno Beads p50-Tau
847-060100030[x]	Immuno Beads brain derived Tau
847-060100040[x]	Immuno Beads Beta-Amyloid

## ELISAs for Tau protein

Order number	Description	Quantity
847-0108000101	hTAU total ELISA	12x8 reactions
847-0108000104	phosphoTAU ELISA	12x8 reactions
847-0108000102	non-pTAU ELISA	12x8 reactions
847-0104000112	p231 TAU ELISA	12x8 reactions
847-0104000116	TAU AGGREGATE ELISA	12x8 reactions

## Antibodies for Tau protein & beta-Amyloid

Order number	Clon	Reactivity
[x] = [1]: 100 µg, [3]: 1 mg		
847-010200380[x]	1E7	Phospho-Tau (Thr181)
847-010200390[x]	8B11	Phospho-Tau (Thr181)
847-010200620[x]	8D2	Phospho-Tau (Thr181)
847-010200610[x]	10D3	Phospho-Tau (Thr181)
847-010200860[x]	14B6	Phospho-Tau (Thr181) <b>NEW</b>
847-010200320[x]	1F3	Phospho-Tau (Ser199)
847-010200460[x]	9C8	Phospho-Tau (Ser199+Ser202)
847-010200450[x]	10F8	Phospho-Tau (Ser202)
847-010200350[x]	2B11	Phospho-Tau (Thr231)
847-010200360[x]	5G7	Phospho-Tau (Thr231)
847-010200370[x]	9D8	Phospho-Tau (Thr231)
847-010200310[x]	4C10	Phospho-Tau (Thr231)
847-010200440[x]	3G3	Phospho-Tau (Thr231+Ser235)
847-010200800[x]	15E3	Phospho-Tau (Thr50) <b>NEW</b>
847-010200480[x]	4B5	Tau-441 (2N4R)
847-010200510[x]	8F10	Tau-441 (2N4R)
847-010200520[x]	12C2	Tau-441 (2N4R)
847-010200530[x]	18B5	Tau-441 (2N4R)
847-010200630[x]	7E5	Tau all isoforms
847-010200640[x]	2B6	Exon 3 human Tau
847-010200660[x]	9E11	Exon 2 and 3 human Tau
847-010200760[x]	2B8	Brain-derived Tau <b>NEW</b>
847-010300100[x]	polyclonal	Tau-441 (2N4R)
847-010200650[x]	6D11	Beta-Amyloid
847-010200840[x]	2C7	Beta-Amyloid 1-12
847-010200850[x]	3C4	Beta-Amyloid 1-12

## Tau proteins

Order number	Description
[x] = [1]: 100 µg, [2]: 500 µg; [3]: 1 mg	
847-010100900[x]	Tau-441, (2N4R), P301L mutant



# Prion protein

Several human degenerative diseases appear as result of misfolding and aggregation of proteins. The prototype central nervous system proteinopathy is CJD, in which neuronal prion protein (PrP) with high  $\alpha$ -helical content switches into a stable structure rich in  $\beta$ -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.

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 clinical practice in addition to the current classic biomarkers.



[3] Dorey et al. (2015) JAMA Neurol. doi:10.1001/ jamaneurol.2014.4068



# Order Information

## ELISAs for Prion Protein

Order number	Description	Quantity
847-0104000104	BetaPrion® HUMAN ELISA	12x8 reactions
847-0104000103	BetaPrion® SCRAPIE ELISA	12x8 reactions

## Antibodies for Prion Protein

Order number	Clon	Reactivity
[x] = [1]: 100 µg, [3]: 1 mg; * 50 µg		
847-010200120[x]	5C4	Human, cattle, sheep, and deer prion protein
847-010200130[x]	1E2	Human and cattle prion protein
847-010200150[x]	6G3	Human, cattle, sheep, and deer prion protein
847-010200160[x]	5B9	Human and cattle prion protein
847-010200410[x]	6E2	Human and cattle prion protein
847-010200420[x]	7D5	Human and cattle prion protein
847-010200430[x]	5G11	Human and cattle prion protein
847-0102001704*	14D11	Human, sheep, and cattle prion protein, PrP <sup>res</sup>
847-010200070[x]	4F7	Bovine and human prion protein, PrP <sup>res</sup>
847-010200080[x]	1E5	Bovine and human prion protein, PrP <sup>res</sup>
847-010200090[x]	3E7	Bovine, human, and ovine prion protein, PrP <sup>res</sup>
847-010200100[x]	3B8	Bovine and ovine prion protein, PrP <sup>res</sup>
847-010200110[x]	7B6	Bovine, human, sheep, and deer prion protein
847-010300010[x]	pAB R10 polyclonal	(sheep, human, cattle, deer, and mouse) prion

## Prion proteins

Order number	Description
[x] = [1]: 100 µg, [2]: 500µg [3]: 1 mg	
847-010100010[x]	Recombinant bovine prion protein
847-010100030[x]	Recombinant human prion protein
847-010100060[x]	Recombinant sheep prion protein
847-010100070[x]	Recombinant deer prion protein



## $\alpha$ -Synuclein

$\alpha$ -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  $\alpha$ -Synuclein are the main components of Lewy bodies (LB), which are intracellular inclusions characteristic for certain neurodegenerative diseases referred to as  $\alpha$ -synucleinopathies. These include Parkinson's disease (PD), Parkinson's disease dementia (PDD), dementia with Lewy bodies (DLB) and multiple system atrophy (MSA).

However,  $\alpha$ -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, ROBOSCREEN provides an improved ELISA for detection of total human  $\alpha$ -Synuclein. Additionally, the discrimination of total  $\alpha$ -Synuclein and disease-specific  $\alpha$ -Synuclein is of special interest for distinguishing between different patient groups.

The Anti-human  $\alpha$ -Synuclein 5G4, monoclonal antibody strongly binds to the high molecular weight fraction of  $\beta$ -sheet rich oligomers, while no binding to primarily disordered oligomers or monomers is observed. This outstanding capability is used for the HUMAN  $\alpha$ -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. We have established monoclonal antibodies as tools for research and diagnostic of neurodegenerative disorders [4;5]. Moreover, NEW hTDP43 total ELISA using antibody 21B2 directed to N-terminal part of the molecule and 2G10 recognizing the middle region of the protein quantifies TDP43 in CSF as well as blood plasma. This ELISA shows very promising results in discrimination between AD, FTD, PDD and DLBD patients in combination with our non-pTAU ELISA.

[4] Fourier (2019) Anal. Bioanal. Chem. doi: 10.1007/ s00216-018-1437-4

[5] Calderón-Garcidueñas et al. (2020) Environ Res. doi: 10.1016/j.envres.2020.110139



# Order Information

## ELISAs for alpha-Synuclein

Order number	Description	Quantity
847-0108000103	hSYN total ELISA	12x8 reactions
847-0104000108	HUMAN alpha-Synuclein PATHO ELISA	12x8 reactions

## Antibodies for alpha-Synuclein

Order number	Clon	Reactivity
[x] = [1]: 100 µg, [3]: 1 mg 847-010200180[x]	10C3	Human α-synuclein
847-010200400[x]	5G4	β-sheet oligomers of human α-synuclein
847-010200470[x]	10D2	Human α-synuclein
847-010300090[x]	polyclonal	Human α-synuclein

## Recombinant alpha-Synuclein

Order number	Description
[x] = [1]: 100 µg, [2]: 500µg [3]: 1 mg 847-010100850[x]	Human α-synuclein, His-tagged
847-010100860[x]	Human α-synuclein

## ELISAs for TDP43

Order number	Description	Quantity
847-0108000107	hTDP43 total ELISA	12x8 reactions

## Antibodies for TDP43

Order number	Clon	Reactivity
[x] = [1]: 100 µg, [3]: 1 mg 847-010200740[x]	2G10	TDP43 (200-220)
847-010200770[x]	21B2	TDP43 (80-90)
847-010200780[x]	19C9	TDP43 (80-90)
847-010200790[x]	35G7	TDP43 (260-270)
847-010200810[x]	1E6	Phospho-TDP43 (Ser409/410)
847-010200820[x]	2F11	Phospho-TDP43 (Ser409/410)
847-010200820[x]	11C10	Phospho-TDP43 (Ser409/410)





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