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

Neuro IP Kit

Pre-analytical Enrichment of AD biomarkers from plasma

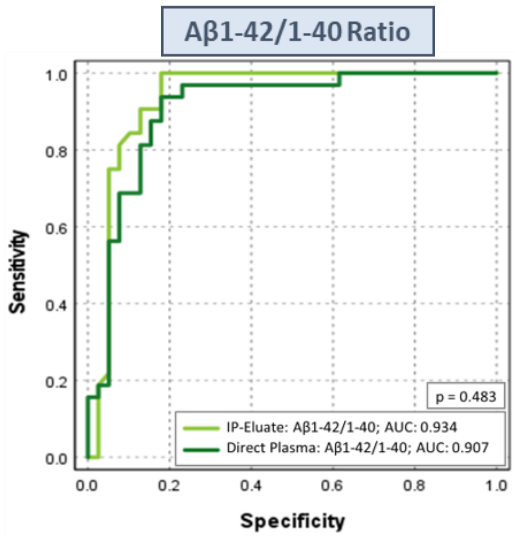
The increasing number of AD cases worldwide calls for advancing the low-invasive and low-cost plasma analysis of AD pathology biomarkers. But these biomarkers are only found in small amounts in plasma, making them difficult to measure. The Neuro IP Kit enables the enrichment of AD relevant proteins such as total Tau, the brand-new markers p50-Tau and brain-derived Tau as well as beta-Amyloid (Aβ) 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, beta-Amyloid, total α-Synuclein and patho-oligomeric α-Synuclein. We can also provide automation solutions for the Neuro IP Kit – Contact us to find the optimal application solution for you.

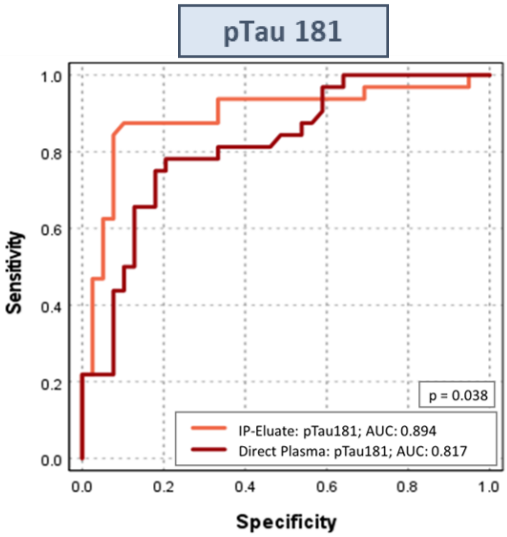
Combinable with mAb coupled immunobeads for the target of your choice

total Tau
p50-Tau
beta-Amyloid
brain-derived Tau
total α-Synuclein
patho-oligomeric α-Synuclein

Measurement of plasma pTau181 and Aß42/40 on the Lumipulse G System with and without pre-analytical sample workup by magnetic bead immunoprecipitation showed great compatibility of the Neuro IP Kit with the Lumipulse platform. Pre-analytical Tau-IP improved the diagnostic contrast significantly (p=0.038). (The data presented here are from AD/PD 2023 Poster #368 by Barbara Morgado, a member of Jens Wiltfang's group, University Goettingen).



Pre-analytical Aß-IP increased the area under the ROC curve (AUC) for plasma Aß42/40 from 0.907 to 0.934 (p=0.48)



Pre-analytical Tau-IP increased the AUC for pTau181 significantly from 0.817 to 0.894 (p=0.038)

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 (Aβ42) and a low ratio of Aβ42 to beta-Amyloid 1-40 (Aβ42/Aβ40), 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 as 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 off 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

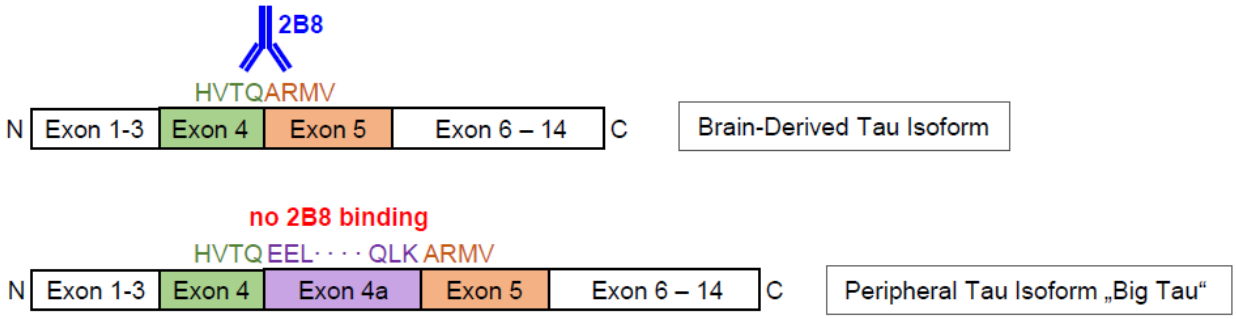
Brain-derived Tau

Anti-human TAU total mAb 2B8

Specificity: human TAU441 (2N4R) amino acids 121-128

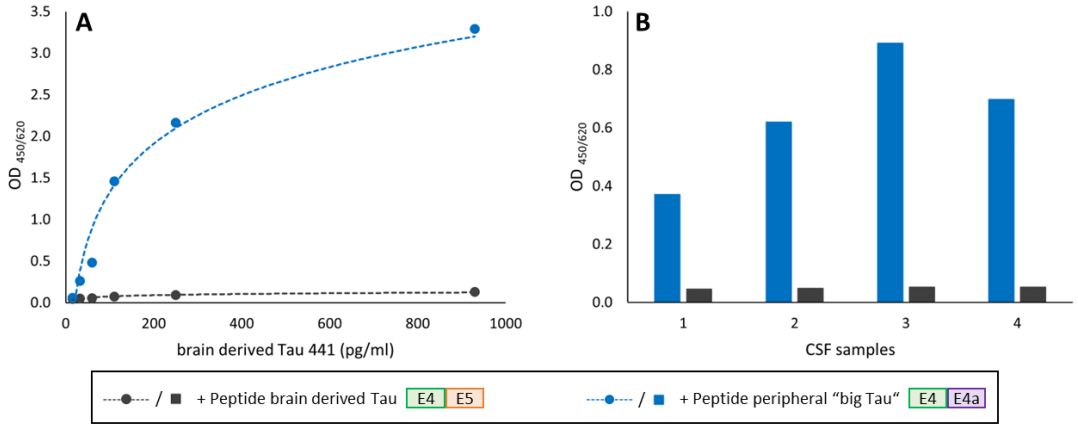
➔ mAb 2B8 selectively binds to continuous exon 4-5 sequences on brain-derived Tau isoforms, but not to peripheral „Big Tau" isoforms containing the exon 4a insert

Schematic Illustration of the peripheral Tau isoform („Big Tau") including Exon 4a and the brain-derived Tau isoform lacking Exon 4a:



Competitive ELISA

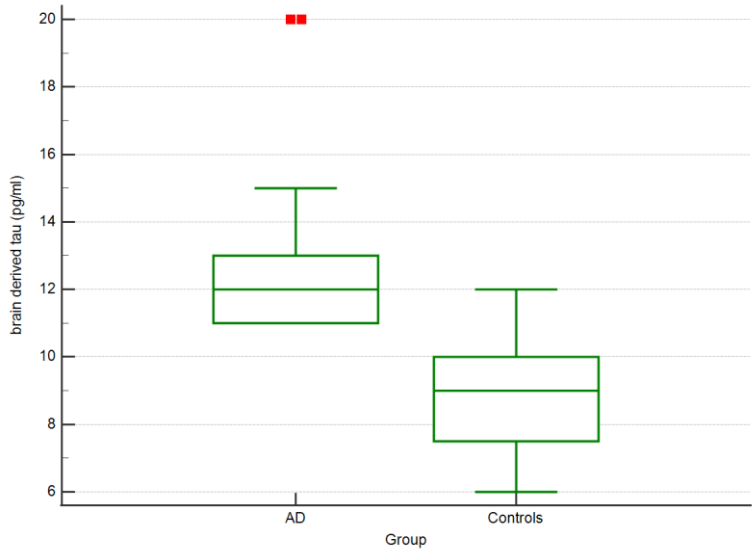
Brain-derived Tau binding by 2B8 is completely inhibited by its recombinant antigen comprising the exon 4-5 junction.



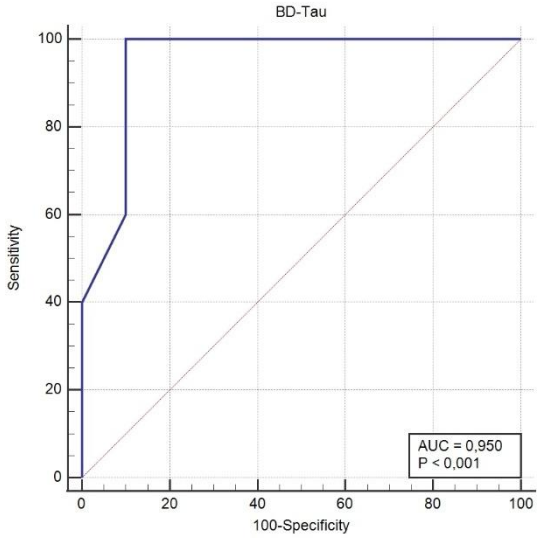
Anti-human Tau total mAb 2B8 used as capture Ab in a Sandwich ELISA is not inhibited by a recombinant peptide comprising the exon 4-4a junction (E4-E4a), however, complete inhibition of mAb 2B8 by a recombinant peptide comprising the exon 4-5 junction (E4-E5) is observed (Figure A). The binding of tau protein from cerebrospinal fluid (CSF) is not affected by the presence of peptide E4-E4a; in contrast, the binding of brain derived CSF tau by mAb 2B8 no longer occurs in the presence of the peptide E4-E5 (Figure B).

BD-Tau Luminescence ELISA combined with pre-analytical enrichment of Tau Neuro IP from plasma samples shows excellent differentiation between Alzheimer and control patients

Pre-analytical enrichment of Tau from plasma samples with the Neuro IP-Kit (847-0108000108) and subsequent measurement of brain-derived Tau using an in-house Luminescence ELISA shows excellent differentiation between Alzheimer´s disease (AD, n = 20) and control patients (Control, n = 20).



Tau Neuro IP from 500 µl plasma of AD (n = 20) and control (n = 20) patients with subsequent measurement of the eluates with an in-house BD-Tau Luminescence ELISA shows excellent discrimination between the AD and control group.



ROC analysis for brain-derived Tau of AD (n = 20) and control (n = 20) patients shows an AUC of 0.95 (p<0.0001).

p50-Tau

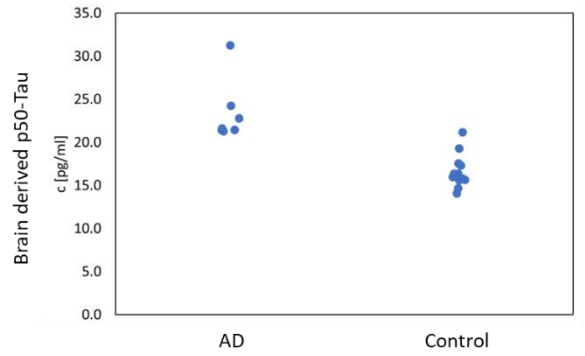
Anti-human phosphor-50 TAU mAb 15E3

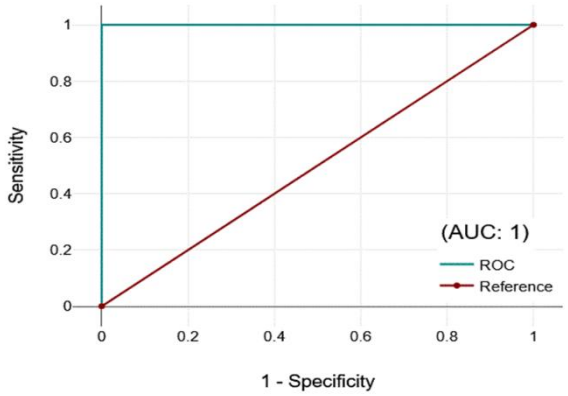
Specificity: human TAU phosphorylated at amino acid position 50 (T)

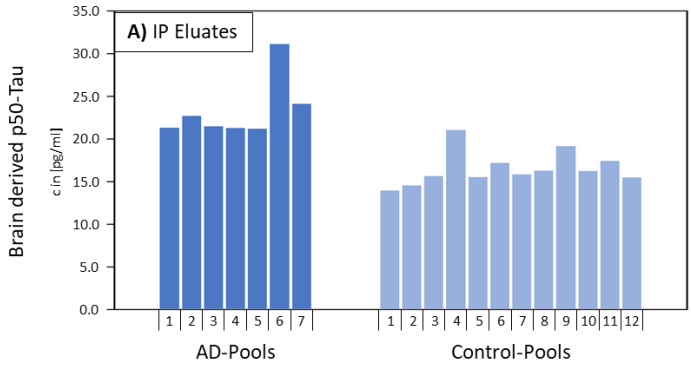
➔ p50 is a master phosphorylation site

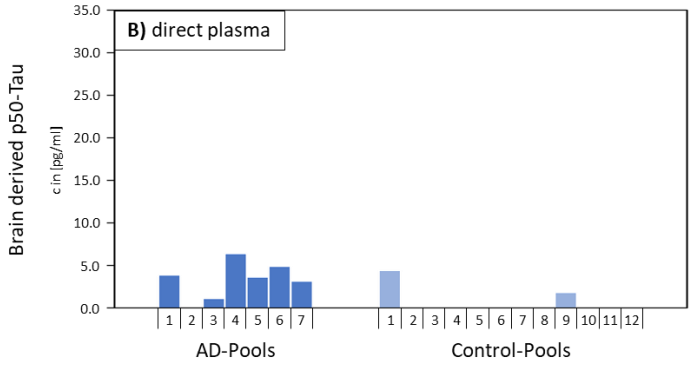
P50-Tau has the potential to distinguish AD from control patients

Pre-analytical enrichment of Tau from Plasma samples with the Neuro IP-Kit (847-0108000108) and subsequent measurement of threonine-50 phosphorylated, brain derived Tau (p50-BD-Tau) in an in-House SIMOA Assay shows excellent differentiation between Alzheimer (AD-Pools*, n=7) and Controls (Control-Pools**, n=12).









Pre-analytical enrichment of Tau from Plasma samples by magnetic bead immunoprecipitation (A) with the Neuro IP-Kit (847-0108000108) clearly improves diagnostic measurability in contrast to direct measurement from plasma (B).

Order Information

Pre-analytical Enrichment of AD biomarkers from plasma NEW

Order number [x] = [1]: 6x IP, [2]: 24x IP	Description
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
847-060100050[x]	Immuno Beads human patho-oligomeric alpha-Synuclein
847-060100060[x]	Immuno Beads human total alpha-Synuclein

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 [x] = [1]: 100 µg, [3]: 1 mg	Clon	Reactivity	
Phospho-Tau (Thr50)			
847-010200800[x]	15E3	p50 Tau (Thr50)	
Phospho-Tau (Thr181)			
847-010200860[x]	14B6	p181 Tau (Thr181)	
847-010200930[x]	7B8	p181 Tau (Thr181)	NEW
847-010200960[x]	7B9	p181 Tau (Thr181)	NEW
Phospho-Tau (Ser199/Ser202)			
847-010200320[x]	1F3	p199 Tau (Ser199)	
847-010200460[x]	9C8	p199/p202 Tau (Ser199+Ser202)	
847-010200450[x]	10F8	p202 Tau (Ser202)	
Phospho-Tau (Thr217)			
847-010200880[x]	9G8	p217Tau (Thr217)	NEW
Phospho-Tau (Thr231/Ser235)			
847-010200350[x]	2B11	p231Tau (Thr231)	
847-010200360[x]	5G7	p231Tau (Thr231)	
847-010200370[x]	9D8	p231Tau (Thr231)	
847-010200870[x]	8G5	p231Tau (Thr231)	
847-010200440[x]	3G3	p231/235Tau (Thr231+Ser235)	
847-010200910[x]	5C4	p231Tau (Thr231)	NEW
847-010200920[x]	6D2	p231Tau (Thr231)	NEW
847-010200940[x]	7D11	p231Tau (Thr231)	NEW
847-010200950[x]	2B5	p231Tau (Thr231)	NEW
Brain derived Tau			
847-010200760[x]	2B8	Brain-derived Tau	
Pan-Tau			
847-010200630[x]	7E5	Tau all isoforms	
847-010200510[x]	8F10	Tau all isoforms	
Tau Isoforms			
847-010200640[x]	2B6	Exon 3 human Tau	
847-010200660[x]	9E11	Exon 2 and 3 human Tau	
Beta-Amyloid			
847-010200650[x]	6D11	Beta-Amyloid N-terminus	
847-010200840[x]	2C7	Beta-Amyloid 1-12	
847-010200850[x]	3C4	Beta-Amyloid 1-12	
847-010200890[x]	22C2	Beta-Amyloid 42	
847-010200900[x]	RS-07	Beta-Amyloid N-terminus	NEW

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 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.

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 [x] = [1]: 100 µg, [3]: 1 mg; * 50 µg	Clon	Reactivity
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^{res}
847-010200070[x]	4F7	Bovine and human prion protein, PrP^{res}
847-010200080[x]	1E5	Bovine and human prion protein, PrP^{res}
847-010200090[x]	3E7	Bovine, human, and ovine prion protein, PrP^{res}
847-010200100[x]	3B8	Bovine and ovine prion protein, PrP^{res}
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 [x] = [1]: 100 µg, [2]: 500µg [3]: 1 mg	Description
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

α-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, ROBOSCREEN provides an improved ELISA 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.

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. 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 [x] = [1]: 100 µg, [3]: 1 mg	Clon	Reactivity
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 [x] = [1]: 100 µg, [2]: 500µg [3]: 1 mg	Description
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 [x] = [1]: 100 µg, [3]: 1 mg	Clon	Reactivity
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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