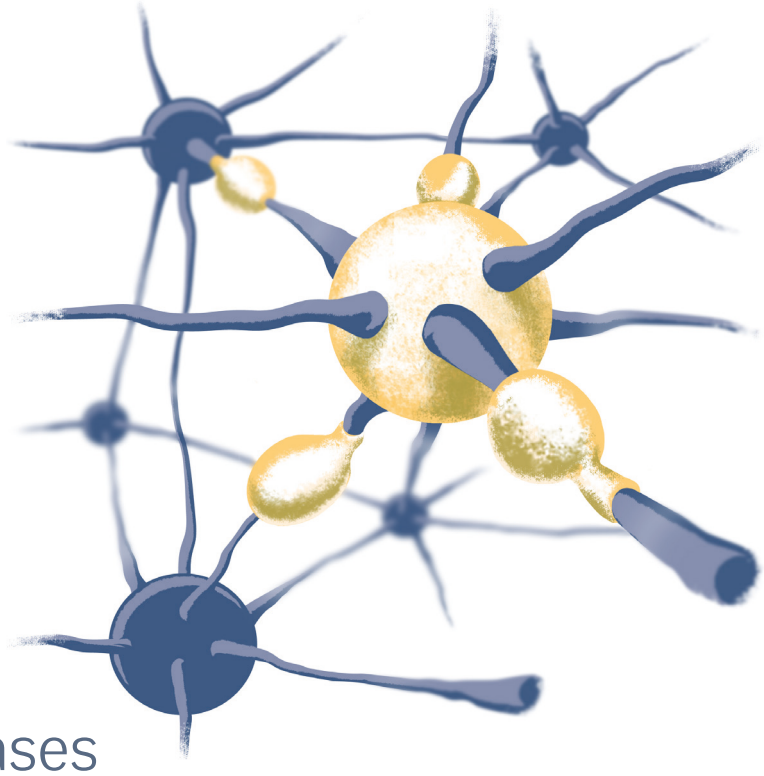
IBL INTERNATIONAL

Neurodegeneration / Neurotransmitters | Method ▽ | here you GO!

- Catecholamines / Neurotransmitters
- Amyloids & others



Neurodegenerative diseases

The largest selection of ELISAs and antibodies for research

Neurodegenerative diseases are caused by the progressive loss of structure or function of neurons, including neuronal death. There are currently millions of people suffering from Alzheimer's disease, Parkinson's disease, multiple sclerosis and amyotrophic lateral sclerosis, and the incidence is expected to soar as the population ages. For this reason, improving diagnostic evaluations and finding novel treatments has become a high-priority goal.

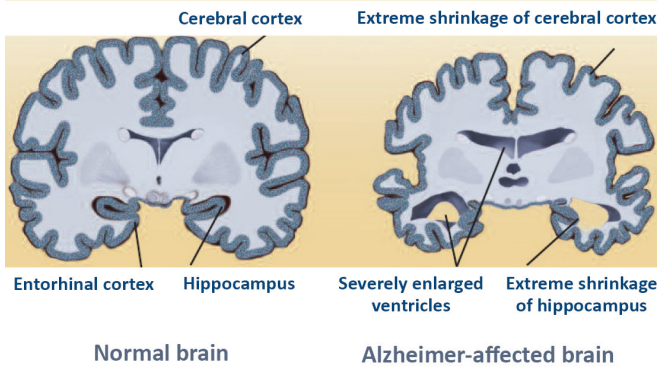
At the heart of Alzheimer's disease research

Alzheimer's disease (AD) is the most common cause of dementia in the elderly, currently affects over 30 million people worldwide. It is characterized by 3 pathological hallmarks: (1) AD patients show characteristic protein deposits, the so-called amyloid-β plaques between the neurons in the brain. (2) Deposits of neurofibrillary tangles composed of hyperphosphorylated microtubule-associated protein tau are found inside the neurons; (3) The brain of an AD patient has considerably less volume due to neuronal and synaptic loss.

Altered levels of Aβ (1-42) and tau in cerebrospinal fluid (CSF) are generally accepted as early indicators of AD in humans.

Assays and antibodies for animal and human studies

Through its partnership with prominent centers, IBL International boasts over 15 years' experience in AD research and provides the most comprehensive portfolio of ELISAs and antibodies, many of which are unique, for AD research in animal models and humans.



Amyloid-β precursor protein: The origin of amyloid-β

Amyloid-β precursor protein (APP) is a single-pass (type 1) transmembrane protein of approximately 120 kDa, ubiquitously expressed in mammalian cells. APP is involved in synapse formation and function. It is the precursor molecule of amyloid-β, whose fibrillary form is the primary component of the plaques found in the brain of AD patients. Mutations in APP are associated with early-onset autosomal dominant AD. For example, the Swedish mutation of APP (codon 670/671) leads to a 6-fold increase in amyloid-β production.

Products

- sAPPβ wild type ELISA
- sAPPβ Swedish type ELISA
- sAPPα ELISA
- sAPPα mouse/rat ELISA
- sAPPtotal ELISA
- APPβ-CTF ELISA
- APP770 ELISA (unique!)

The amyloid-β cascade: From APP to amyloid-β plaques

APP is processed, inter alia, by cleavage by α-secretase in its extracellular region (non-amyloidogenic pathway). Alpha secretases are members of the ADAM ('a disintegrin and metalloprotease domain') family, expressed on cell surfaces and anchored to the plasma membrane. Upon cleavage by α-secretases, APP releases its extracellular domain, a fragment known as sAPPα, into the extracellular environment in a process known as ectodomain shedding (Lammich S. et al. PNAS. 1999; 96(7):3922-7).

AD-related Aβ peptides are generated when APP is instead processed by β-secretase and γ-secretase. Two sequential cleavages are required. The initial extracellular cleavage of APP by beta-secretase 1 (BACE1) creates a soluble extracellular fragment and a cell membrane-bound fragment referred to as C99. Cleavage of C99 within its transmembrane domain by γ-secretase releases the intracellular domain of APP and generates Aβ.

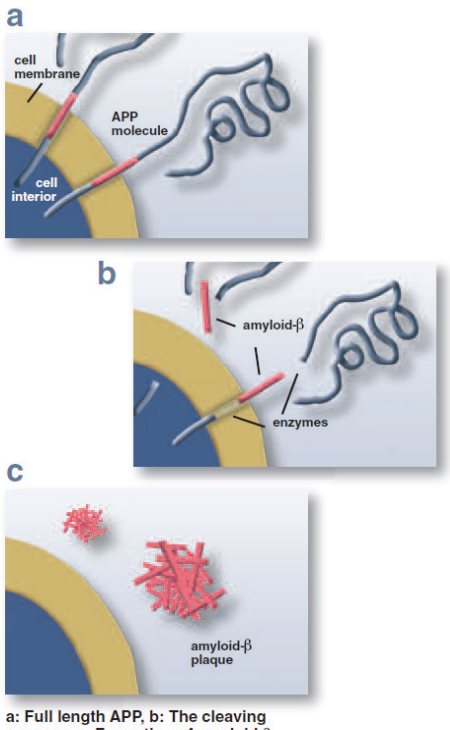
It is generally accepted that Aβ (1-42) is a major constituent of amyloid plaques, and its formation by various β- and γ-secretases is well understood. Apart from the known neurotoxicity of Aβ (1-42), the role of the majority of the Aβ isoforms is still unclear. Recently, several publications proposed a prominent role of Aβ (1-43), contending that it is more neurotoxic than Aβ (1-42) (Saito T. et al. Nat Neurosci. 2011; 14(8):1023-32 | Takami M. et al. J Neurosci. 2009; 29(41): 13042-52 | Zou K. et al. Am J Pathol. 2013; 182(6):2322-31 | Sandebring A. et al. PLoS One. 2013;8(2):e55847).

Amyloid-β isoforms in transgenic animals

Transgenic animals expressing mutated APP and tau have been made to closely recapitulate the human neuropathology of AD. They are valuable models for developing novel therapeutic modalities. However, these models are prone to endogenously developing pathologies. Therefore, studying Aβ and treatment responses requires reliable methods of measuring respective endogenous amyloid-β isoforms.

Products

- Amyloid-β (1-43) ELISA – (unique!)
- Amyloid-β (1-42) ELISA
- Amyloid-β (1-42) (N) ELISA
- Amyloid-β (1-40) ELISA
- Amyloid-β (1-40) (N) ELISA
- Amyloid-β (1-40) (FL) ELISA
- Amyloid-β (1-42) mouse/rat ELISA
- Amyloid-β (1-40) highly-specific mouse/rat ELISA
- Amyloid-β Oligomers ELISA
- Amyloid-β (1-38)(FL) ELISA – (unique!)
- Amyloid-β (1-x) ELISA
- BACE1 ELISA
- α2,6-Sialyltransferase ELISA



a: Full length APP, b: The cleaving process, c: Formation of amyloid-β plaque.

PyroGlu-Aβ:
The seed for plaque formation

In 1995, it was discovered that the main components of Aβ plaques are N-truncated and modified Aβ fragments (primarily Aβ3 (pE)-42 and Aβ3 (pE)-40, (cf. Saido T.C et al., Neuron 1995; 14(2): 457-66).

These fragments are predominantly found in the central regions of the plaque, which has raised the hypothesis that these fragments may act as a seed, stimulating the aggregation of other Aβ fragments.

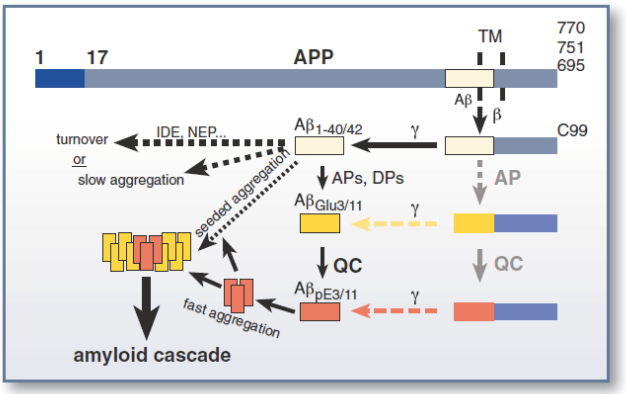
The formation of pyroglutamate Aβ ("pyroGlu-Aβ") is mediated by glutaminyl cyclase (QC). QCs catalyze the formation of pyroglutamate (pGlu) from N-terminal glutamine or glutamic acid residues of a number of peptide hormones, neuropeptides and chemokines. This post-translational modification stabilizes these peptides; it protects them from proteolytical degradation or is important for their biological activity. It has been shown that the inhibition of stabilization of Aβ3E-42 leads to reduced plaque formation (Cynis H. et al. Biochim Biophys Acta 2006; 1764(10):1618-25 | Schilling S. et al. J Neurochem 2008; 106(3):1225-36 and Nat Med 2008; 14(10):1106-11).

Products

Amyloid-β (N3pE-42) ELISA – (unique!)

Amyloid-β (N3pE-40) ELISA – (unique!)

Anti-human amyloid-β (N3pE) rabbit IgG antibody



According to Schilling S, et. al., Nat Med 2008; 14(10):1106-11.

Inflammation:
A new target in AD research

Glutaminyl cyclase (QC) has been shown to be a major enzyme in inflammatory processes. This has linked AD to inflammation. Over the last few years, this has led to a completely new approach to AD research. The impact of inflammation and the subsequent involvement of the immune system in the development of AD are now being studied.

A major protein involved in inflammatory processes is HMGB1. Recently, a Japanese study group reported that HMGB1 is responsible for dysfunctional clearance (phagocytosis) of the amyloid-β (1-40) isoform (Takata K et al. Int J Alzheimers Dis. 2012; 2012: 685739).

Products

HMGB1 ELISA

Anti-HMGB1 antibodies

Chemokine-HMGB1 protein, HMGB2 protein

Cytokine-HMGB1 protein

BoxA, BoxB from HMGB1

Biomarkers:
Early diagnosis of Alzheimer's disease

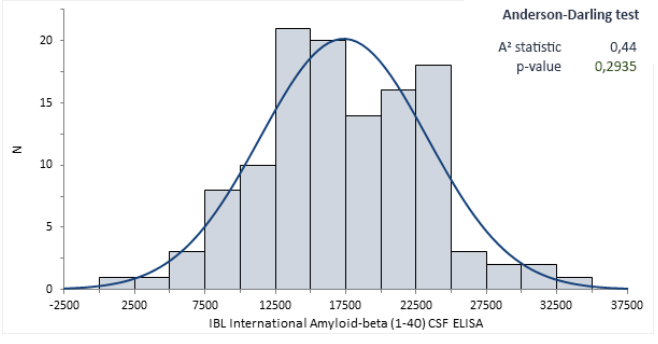
Both the CSF Aβ and tau measurements are part of the diagnostic criteria laid down by the US National Institutes of Health (NIH).

The novel IBL International ELISAs for assessing Aβ and tau levels in human CSF show a superb analytical performance (assay specificities, linearity, precision, recovery, etc.).

The Aβ ELISAs were specifically designed to allow for the splitting of one diluted CSF sample and using the same protocol for both assays. This is a major improvement over other currently available assays for establishing the Aβ 42/40 ratio.

Amyloid-β (1-42)

In recent years it has become common practice to measure Aβ42 as an aid to the early diagnosis of AD. Hypothesis-driven evidence suggests that the CSF concentration of Aβ (1-42) peptide depends not only on the physiologic status of a person (i.e. the presence or absence of an underlying amyloid pathology) but also on the person's total amount of Aβ peptides. This may reflect different efficiency in the processing of APP molecules by β-secretase in different people. Correspondingly, intralaboratory assessment of 82 patient samples showed that amyloid-beta (1-40) followed a nearly Gaussian distribution.



Consequently, normalization of the Aβ (1-42) concentration for the total amount of Aβ peptides (or their most abundant isoform, Aβ (1-40)) by using the Aβ 42/40 ratio was found to improve the sensitivity and specificity of the AD diagnosis as compared to using the CSF Aβ (1-42) concentration alone (Wiltfang et al. J Neurochem. 2007; 101(4): 1053-9).

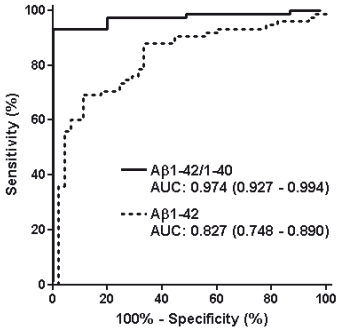
Products

Amyloid-β (1-42) CSF ELISA – CE-marked

Amyloid-β (1-40) CSF ELISA – CE-marked

Tau total ELISA – CE-marked

Simultaneously measuring the two Aβ isoforms using the novel IBL International Aβ ELISAs confirmed that the CSF Aβ 42/40 concentration ratio displays a significantly better diagnostic performance compared to measuring the CSF Aβ (1-42) concentration alone. The amyloid beta ratio is more diagnostically conclusive (significance of p>0.0001) than the determination of amyloid beta (1-42) alone (Lewczuk et.al. J Alzheimer Dis. 2014).



Tau

Increases in total Tau CSF concentrations are thought to reflect non-specific disruptions of nerve cells; abnormal hyperphosphorylation of tau is a hallmark of AD and hyperphosphorylated tau molecules form neurofibrillary tangles.

Furthermore, the determination of total tau as a marker of tau pathology in Alzheimer's disease is also widely accepted. The combination of markers for amyloid beta pathology and tau pathology significantly increases the diagnostic sensitivity and specificity. Known combination principles here are, inter alia, the Hulstaert and Rösler criteria. The AD-CSF-index was presented this year at the Alzheimer's Association International Conference (AAIC) as a novel method.

Dementia: It's not only Alzheimer's disease

Dementia is the term used to describe the symptoms of a number of illnesses that affect the brain. Their shared clinical feature is cognitive decline.

Dementias can be divided into cortical dementias, meaning disorders affecting the cerebral cortex, and sub-cortical dementias, signifying the malfunction of brain areas beneath the cerebral cortex.

Primary cortical dementias besides AD are vascular dementia, frontotemporal lobar degeneration (FTLD), dementia with Lewy bodies (DLB) and Creutzfeldt-Jakob disease (CJD).

Sub-cortical dementias include conditions such as Huntington's disease, Parkinson's disease and AIDS dementia complex (ADC).

Products

Dopamine ELISA

Prion protein ELISA

Anti-human CRMP-2 (C4G) mouse IgG antibody

Anti-human CRMP-2 (N3E) IgG antibody

Anti-human CRMP-2 (phosphorylated) (3F4) mouse IgG antibody

Anti-mouse Fez1 (F441) rabbit IgG antibody

Anti-human Olig2 rabbit IgG antibody

Anti-human Parkin (1A1) mouse IgG antibody

Anti-human Parkin (5A1) mouse IgG antibody

Anti-human presenilin-1 (17C2) mouse IgG antibody

and many more…

Neurofilament light: A marker for axonal damage

Neurofilaments are the backbone of the neuronal cytoskeleton. Inside the axons, phosphorylation and dephosphorylation of the neurofilaments regulate the expansion and contraction of the microtubules, respectively. The neurofilament light chain (NFL) is the stoichiometrically most common form compared to the medium (NFM) and heavy (NFH) chain isoforms.

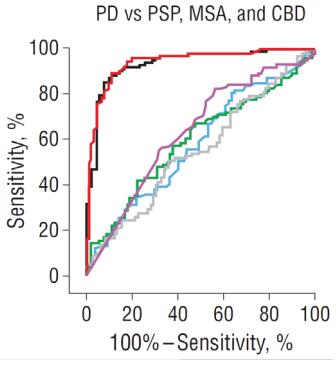
NFL levels are found to be elevated in neurodegenerative disorders that are associated with the destruction of the white matter such as:

- Parkinson's disease (PD)
- Multiple sclerosis (MS)
- Amyotrophic lateral sclerosis (ALS; Lou Gehrig's disease)

IBL International provides the NF-Light® (neurofilament light) ELISA that enables a rapid (3-hour) quantification of neurofilament light chain.

NFL in Parkinson's and related diseases

The ROC curve shows that NFL (red) can differentiate the atypical Parkinsonian syndromes such as progressive supranuclear palsy (PSP), multiple system atrophy (MSA) and corticobasal degeneration (CBD) from Parkinson's disease (PD) with an AUC of 0.93 (95% CI, 0.89-0.97). The black curve represents an algorithm of all 5 biomarkers measured in this study (NFL, α-Syn, Tau, p-Tau181 , Aβ42), indicating that it is dominated by NFL (Hall S. et al. Arch Neurol. 2012 Nov; 69(11):1445-52).

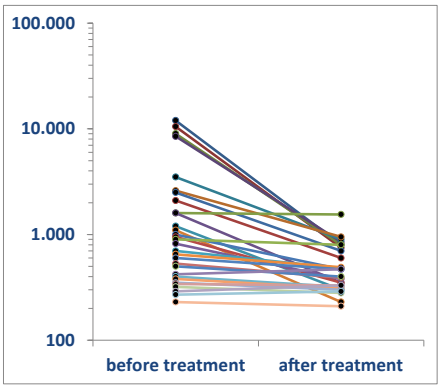


Products

NF-Light® (Neurofilament light) ELISA

NFL in multiple sclerosis

It has been shown that NFL has a significantly better discriminatory power than the NF-heavy chain in the diagnosis of clinically isolated syndrome (CIS) and any other MS subtype. Using NFL, it is possible to differentiate between the patients and apparently healthy controls with an AUC of 0.83 (Kuhle J. et al. Mult Scler. 2013 Oct; 19(12):1597-603). Additionally, NFL is also a tool used to monitor treatment. It has been shown that NFL values decrease after Natalizumab treatment compared to the pre-treatment NFL values (Tortelli R. et al. Eur J Neurol. 2012 Dec;19(12):1561-7).



NFL in amyotrophic lateral sclerosis

An italian study group has shown that NFL can differentiate the rapidly progressive ALS (PR>0.71/month) from the slowly progressive ALS (PR≤0.71/month) with a high statistical significance ($p<0.0001$). It was also found that NFL can help differentiate ALS from other neurodegenerative diseases (Tortelli R et al. Eur J Neurol. 2012 Dec; 19(12):1561-7).

IBL International is a Tecan Group company

IBL International GmbH
Flughafenstrasse 52a
D-22335 Hamburg
Germany

Phone: +49 (0)40-53 28 91-0
Fax: +49 (0)40-53 28 91-11
Email: IBL@IBL-International.com

Amyloids & others 2014 v01