

Antibodies for Alzheimer's Disease

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by dementia that generally initiates with subtle failure of memory, progressing over years to an incapacitating level. Approximately 25 % of all AD is familial of which approximately 95 % is late-onset (age >60-65 years) and 5 % is early-onset (age <60 years).

The generation of the **Amyloid- β (A β)** peptide through the proteolytic processing of the **Amyloid precursor protein (APP)** is a central event in the pathogenesis of AD. Extracellular accumulation of A β leads to formation of aggregates, fibrils and eventually amyloid deposits called neuritic plaques, a hallmark of AD. The A β peptide has neurotoxic effects and AD research has been focused on determining the underlying mechanisms of A β protein toxicity.

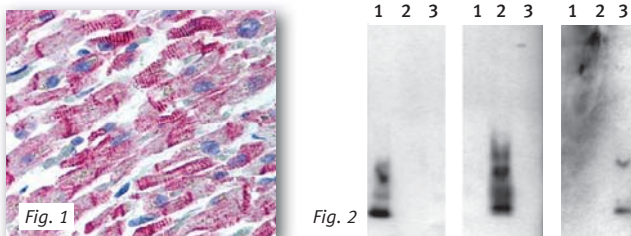


Fig. 1: Formalin-fixed paraffin-embedded (FFPE) heart tissue stained with APP antibody Cat.-No. AP07841PU-N

Fig. 2: Immunoblot analysis with A β 1-40 Cat.-No. AM00001PU-N (left panel), A β 1-42 Cat.-No. AM00003PU-N (middle panel) and A β 1-43 Cat.-No. AM00004PU-N (right panel) (lane 1: A β 1-40; lane 2: A β 1-42; lane 3: A β 1-43)

Established candidates for the cleavage of APP to A β are the β -secretases **BACE1** and **BACE2** and **Presenilin 1 and 2**, which resemble the catalytic subunit of the γ -secretase complex. **PEN2 (presenilin enhancer 2)** is the regulatory component of the γ -secretase complex.

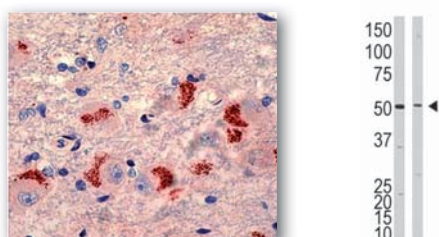


Fig. 3: Presenilin-1 antibody Cat.-No. AP15743PU-N staining of human brain (left). In WB Presenilin 1 antibody Cat.-No. AP13205PU-N was used with mouse kidney tissue lysate (lane 1) and HL60 cell lysate (lane 2)

Ubiquilin 1 (UBQLN1) is a ubiquitin-like protein, which has been shown to play a central role in regulating the proteasomal degradation of various proteins, including the presenilins. A role for UBQLN1 steady-state levels in affecting APP trafficking and processing has been proposed, thereby influencing the generation of A β .

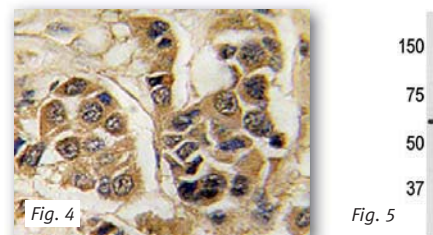


Fig. 4: Human breast carcinoma tissue (FFPE) stained with APPBP2 antibody Cat.-No. AP13997PU-N

Fig. 5: Western blot analysis of APPBP2/PAT1 antibody Cat.-No. AP13998PU-N in HL60 cell line lysates

Amyloid protein-binding protein 1 (APPBP1) and **Amyloid protein-binding protein 2 (APPBP2)** interact with APP and are functionally associated with APP transport and/or processing.

Three alleles for **Apolipoprotein E (ApoE)** are known and there is a strong association of one or two copies of the ApoE allele e₄ with late-onset AD, although the mechanism by which this allele impacts AD remains unproven.

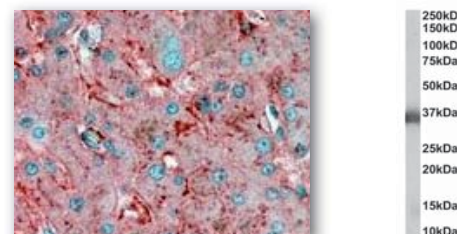


Fig. 6: Detection of ApoE using Cat.-No. AP16344PU-N in human liver tissue (FFPE) (left) and with Western blot of human brain lysate (right)

Apolipoprotein E receptor 2 (ApoER2) is a member of the LDL receptor family that is highly expressed in the brain. It has been shown that ApoER2 expression stimulates A β production by enhanced β - and γ -secretase mediated amyloidogenic processing.

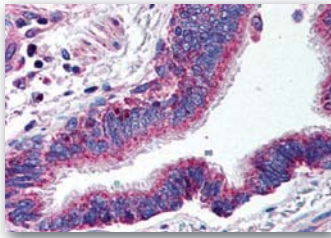


Fig. 7: Lung, respiratory epithelium (FFPE) stained with ApoER2 antibody Cat.-No. AP07359PU-N

Clusterin/apolipoprotein J (Apo J) has also been identified as a potential risk gene in AD. Elevated protein levels are found in the CNS under some neuropathological conditions, such as AD, where Apo J is associated with Aβ plaques.

Microtubule-associated protein tau (MAPT/TAU) is a neuronal microtubule associated protein and it promotes tubulin polymerization and stabilizes microtubules. In its hyperphosphorylated form, tau is the major component of paired helical filaments and neurofibrillary lesions in AD brain. Hyperphosphorylation impairs the microtubule binding function of tau, resulting in the destabilization of microtubules in AD brains, ultimately leading to the degeneration of the affected neurons.

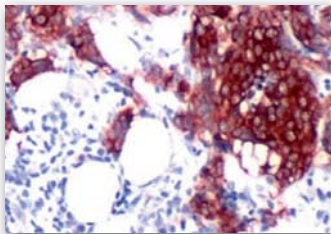


Fig. 8: Paraffin sections of human breast carcinoma stained with MAPT/TAU antibody Cat.-No. AM09107PU-N

Cyclin-dependent kinase 5 activator 1 (CDK5R1) activates CDK5, which is required for proper development of the central nervous system. CDK5R1 is cleaved from a p35 into a p25 form and has been shown to accumulate in neurons of patients with AD. This accumulation correlates with an increase in CDK5 activity and may lead to aberrantly phosphorylated forms of MAPT/TAU, which contributes to AD.

Alpha 1-antichymotrypsin (ACT) has been shown to promote Aβ polymerization and levels of ACT protein in plasma and cerebrospinal fluid from Alzheimer's patients have been found to correlate with progression of dementia. ACT may lead to hyperphosphorylation of tau thereby enhancing degeneration of neurons.

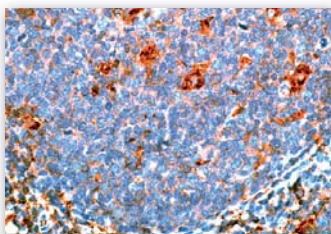


Fig. 9: Human tonsil (FFPE) stained with ACT antibody Cat.-No. AP15343PU-N

Calsenilin and **KCNIP1/VABP** are members of the family of voltage-gated potassium channel-interacting proteins. They interact with presenilin 1 and 2 and are implicated in the mediation of Aβ formation.

Brain-derived neurotrophic factor (BDNF) belongs to so-called neurotrophins and supports the survival of existing neurons and encourages the growth and differentiation of new neurons. Neurotrophins are thought to have a protective role against Aβ toxicity.

Detection of **Neurofilament M** can be used in studies to visualize neurofilament accumulation as it can be seen in AD.

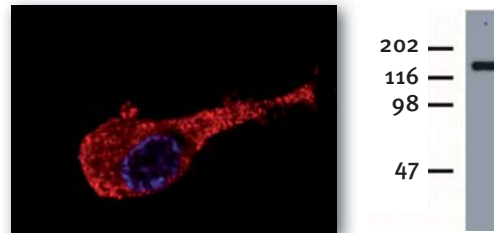


Fig. 10: Immunofluorescence staining of neurofilament M in murine Neuro2A cells (red, DNA stained by Hoechst (blue)) and WB analysis of neurofilament M in porcine brain lysate (reducing conditions) with Cat.-No. SM3068P

In AD, microglial expression of **Macrophage scavenger receptor 1 (MSR1/CD204)** is increased. Findings of CD204 mediated adhesion and endocytosis of fibrillar Aβ by microglia and astrocytes suggest a role for this receptor in neuronal homeostasis and neuropathology.

IL-1 is a cytokine which is overexpressed in the AD brain. This correlates to plaque formation and progression by leading to excessive expression of neuronal APP and other plaque-associated proteins and to nonsensical growth of dystrophic neuritis. Polymorphism in the IL-1A and IL-1B genes are discussed for early age onset AD.

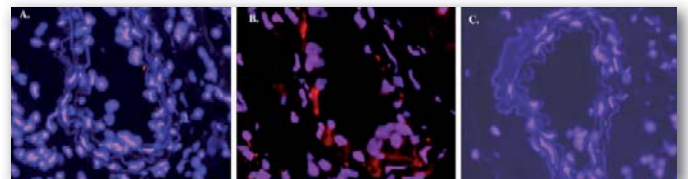


Fig. 11: Immunofluorescence staining of mouse carotid artery tissue (cryo sections) with IL-1B antibody Cat.-No. R1191 (red). Tissue was counterstained with bisbenzamide solution. A) shows no IL-1B staining of WT uninjured mouse carotid tissue. B) shows IL-1B staining of cells after surgical injury of tissue. C) shows no IL-1B staining of injured carotid tissue from an IL-1B KO mouse

Kallikrein-6 is a serin protease and abnormal levels have been found in patients with AD. The potential role of Kallikrein-6 as a biomarker for AD is under investigation and it has been reported that this protein might play a role in the degradation of Aβ or turnover of APP.

Homeobox protein MOX-2 (MEOX2) is a regulator of vascular differentiation and its expression is low in AD. It has been shown that restoring expression of the protein stimulates angiogenesis, suppresses apoptosis and increases the levels of a major Aβ clearance receptor, the low-density lipoprotein receptor-related protein 1 (LRP), at the blood-brain barrier.

Bax, a pro-apoptotic protein belonging to the Bcl-2 family, promotes increased apoptosis leading to enhanced neuronal degeneration in progression of AD. Bax may play a similar role in Huntington's disease.

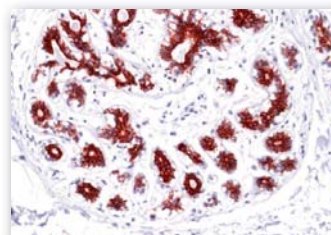


Fig. 12: Paraffin sections of human normal breast tissue stained with Bax antibody Cat.-No. AM11090PU-S



Humanin and its homologue in rats, Rattin, have been shown to suppress the onset of AD-related dementia by inhibiting both AD-related neuronal cell death and dysfunction. Humanin diminishes aggregation and fibrillary formation by suppressing the effect of APP on mononuclear phagocytes and competitively inhibiting the binding of APP to the formyl peptide receptor-like-1 (FPRL1).

While in AD there is abundant evidence for the involvement of oxidative stress, the cause or the consequences are largely unresolved. NAD(P)H dehydrogenase (quinone 1) (NQO1), a redox-regulated flavoenzyme, plays a central role in monitoring cellular redox state and has been shown to be increased in AD.

Recent studies reveal complement component (3b/4b) receptor 1 (CR1) and phosphatidylinositol binding clathrin assembly protein (PICALM) as potential risk genes in AD. Results for CR1 indicate a role in the clearance of A β , but the importance of CR1 and PICALM proteins in AD remains to be elucidated.

Please refer also to other FocusOns about Neurosciences

FocusOn 131: Antibodies for Parkinson's Disease

FocusOn 132: Antibodies for Huntington's Disease

FocusOn 133: Antibodies for Amyotrophic Lateral Sclerosis

Key References

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Hiltunen, M, 2006, J Biol Chem

Husemann, J, 2002, Glia

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Padmanabhan, P, 2006, Brain

Raina AK, 1999, Redox Rep

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Name	Property	Host	Clone	Reactivity	Application	Catalog-No.
ACT		Rabbit		Hu	P, WB	AP15343PU-N
ACT		Mouse	ACT14C7	Hu	C, P	BM4062
Amyloid beta	1–40	Mouse	5C3	Hu	E, IF, WB	AM00001PU-N*
Amyloid beta	1–42	Mouse	8G7	Hu	E, IF, WB	AM00003PU-N*
Amyloid beta	1–43	Mouse	6G12	Hu	E, IF, WB	AM00004PU-N*
Amyloid beta	not APP reactive	Mouse	11H3	Hu	E, WB	AM00005PU-N
Amyloid beta	APP reactive	Mouse	19H5	Hu	E, WB	AM00006PU-N*
ApoE		Rabbit		Ms	ID, WB	BP2046
ApoE		Mouse	E6D7	Hu	C, E, IP, P, WB	AM00810PU-N
ApoE	C-term	Goat		Chimp, Hu	E, P, WB	AP16344PU-N
ApoE	C-term	Rabbit		Hu	E, P, WB	AP14244PU-N
ApoER2/LRP8		Rabbit		Hu	E, P	AP07359PU-N
ApoER2/LRP8	C-term	Rabbit		Hu	E, P, WB	AP13124PU-N
Apo J		Mouse	1A11	Hu	E, P, WB	AM09004PU-S
Apo J		Mouse	Hs-3	Hu	E, IF, P, WB	AM03078PU-N
Apo J		Goat		Hu	C, E, IP, P, WB	R1037P
APP		Rabbit		Hu	IP, P, WB	AP15346PU-N
APP		Rabbit		Hu, Ms, Rt	P, WB	AP15347PU-N
APP		Mouse	J4H9	Hu, Ms	E, P, WB	AM09000PU-N
APP		Rabbit		Hu	E, IF, IP, P, WB	AP07841PU-N
APPBP1	C-term	Rabbit		Hu	E, P, WB	AP13993PU-N
APPBP1	Center	Rabbit		Hu	E, WB	AP13994PU-N
APPBP1	N-term	Rabbit		Hu	E, P, WB	AP13995PU-N
APPBP2	Center	Rabbit		Hu	E, WB	AP13998PU-N
BACE1	N-term	Rabbit		Hu, Ms	E, P, WB	AP14566PU-N
BACE1	Isoform B	Rabbit		Hu, Ms	E, P, WB	AP13066PU-N
BACE1	Isoform C	Rabbit		Hu	E, P, WB	AP13067PU-N
BACE1	Isoform D	Rabbit		Hu	E, P, WB	AP13068PU-N
BACE2		Rabbit		Hu, Ms, Rt	P, WB	AP07871PU-N
BACE2	Center	Rabbit		Hu	E, WB	AP13084PU-N
BACE2	Isoform B, C-term	Rabbit		Hu	E, P, WB	AP13069PU-N
BACE2	Isoform C, C-term	Rabbit		Hu	E, P, WB	AP13070PU-N
Bax		Rabbit		Hu	P	AM11090PU-S
Bax		Mouse	2D2	Hu	IP, P, WB	DM246
Bax	N-term	Rabbit		Hu, Ms, Rt	IP, P, WB	AP08384PU-N

Abbreviations and continuation overleaf



Name	Property	Host	Clone	Reactivity	Application	Catalog-No.
BDNF		Rabbit		Hu, Rt	C, E, FN, WB	PP1000P1*
BDNF		Mouse	NYRhBDNF	Hu	C, E, IP, WB	PM1300
Calsenilin	N-term	Rabbit		Hu, Ms	E, P, WB	AP11608PU-N
Calsenilin		Rabbit		Hu, Ms, Rb, Rt	C	SP5351P
CD204		Goat		Hu	C, E, P, WB	BP2170
CD204		Rat	2F8	Ms	C, E, F, IP, WB	SM029P*
Humanin		Rabbit		Hu	E, WB	SP7377
IL-1A		Mouse		Hu	E, P, WB	AM06011PU-N
IL-1A		Mouse	AS5	Hu	C, E, FN, IP	AM05232PU-N*
IL-1A		Goat		Rt	E, FN, WB	PP1133P1*
IL-1A		Rabbit		Ms	E, FN, WB	PP005P1*
IL-1B		Rabbit		Ms	C, E, FN, IF, IP, P, WB	R1191
IL-1B		Rabbit		Rt	E, FN, WB	PP034P1*
IL-1B		Mouse	AS10	Hu	C, E, FN, IP	AM05234PU-N*
Kallikrein-6	C-term	Goat		Bov, Ms, Rt	E, WB	AP09594PU-N
KCNIP1/VABP		Mouse	39AT957.39.92	Ms	E, WB	AM11024PU-N
KCNIP1/VABP	N-term	Rabbit		Hu, Ms	E, P, WB	AP11606PU-N
MAPT / TAU	C-term	Rabbit		Hu, Ms	E, P, WB	AP11906PU-N
MAPT / TAU	N-term	Rabbit	SP70	Hu	P	AM09107PU-S
MAPT / TAU	pSer416	Rabbit		Bov, Can, Hu, Ms, Rt	WB	AP08750PU-N
MEOX2		Rabbit		Hu, Ms, Rt	E, WB	AP06700PU-N
Neurofilament M		Mouse	3H11	Chk, Hu, Ms, Rt	IF, WB	AM08253SU-N
Neurofilament M		Chicken		Chk, Hu, Ms, Rt	C, IF, WB	AP08697SU-N
Neurofilament M		Mouse	NF-09	All species	IF, P, WB	SM3068P*
NQO1		Goat		Hu, Ms, Rt	WB	SP7251P
NQO1		Mouse	AI80	Hu, Rt	IP, P, WB	AM01393PU-N
PEN2	Center	Rabbit		Hu	E, WB	AP13310PU-N
PEN2	C-term	Rabbit		Hu, Ms, Rt	WB	AP01104PU-N
Presinilin 1	C-term	Rabbit		Hu, Ms	E, P, WB	AP13205PU-N
Presinilin 1	N-term	Rabbit		Hst, Hu, Mky	C	SP1374P
Presinilin 1		Mouse	APS 11	Hu, Mky, Ms, Rt	E, IF, P, WB	SM5161P
Presinilin 1		Rabbit		Hu	P	AP15743PU-S
Presinilin 2	N-term	Rabbit		Hu	E, WB	AP13324PU-N
Presinilin 2		Rabbit		Hu, Mky, Ms, Rt	IF, IP, P, WB	AP20030PU-N
Presinilin 2		Mouse	198C679.2.1	Hu	WB	SM7081
Presinilin 2		Goat		Hu	C, E, P	AP05315SU-N
Presinilin 1+2		Rabbit		Hu	E, P, WB	AP13320PU-N
Presinilin 1+2	C-term	Rabbit		Hu, Ms	E, WB	AP13321PU-N
Rattin	20-35	Rabbit		Rt	WB	AP20031PU-N
Ubiquilin-1 (UBQLN1)	N-term	Rabbit		Hu, Ms	E, P, WB	AP12100PU-N
Ubiquilin-1 (UBQLN1)	Center	Rabbit		Hu, Ms	E, P, WB	AP12101PU-N

Bov: Bovine, Can: Canine, Chimp: Chimpanzee, Chk: Chicken, Hst: Hamster, Hu: Human, Mky: Monkey, Ms: Mouse, Rt: Rat
 C: Immunohistochemistry on frozen sections, E: ELISA, F: Flow cytometry, FN: Functional assay, ID: Immunodiffusion, IF: Immunofluorescence,
 IP: Immunoprecipitation, P: Immunohistochemistry on formalin-fixed, paraffin-embedded tissue sections, WB: Western blot

* Conjugates available