AMYLOID PEPTIDES OFFERED BY BACHEM

Extracellular amyloid-β peptide deposition into cerebellar plaques and formation of intracellular neurofibrillary fibers accompanied by the loss of neurons are characteristic histopathological lesions found in the brains of Alzheimer’s disease patients. Individuals suffering from this disease show a gradual loss of cognitive functions and disturbances in behavior. Apart from some rare familial forms of the disease, the onset of Alzheimer’s disease is usually above 60 years. Since the risk to develop the disease increases with age, Alzheimer’s disease has become a major health and social problem in the developed countries with an increasing proportion of older people. In this brochure we present amyloid peptides and related products for Alzheimer’s disease research.

Alzheimer’s Disease
Alzheimer’s disease (AD) is the prevalent cause of dementia in elderly people and has become one of the leading causes of death in developed countries together with cardiovascular disorders, cancer, and stroke. It is estimated that more than 26 millions of people suffer from AD all over the world.

As age advances, the risk for developing AD increases. The frequency of AD at the age of 60–64 is about 1% and doubles approximately every five years. By the age of 90 and older, approximately 50% of the population suffers from this disease. AD is an irreversible and progressive neurodegenerative disorder. Symptoms include gradual loss of cognitive functions such as memory, verbal and visuospatial abilities, changes in personality, behavior, and activities of daily living. AD patients in the final stages are completely dependent on the care of others.

The characteristic lesions in the brains of AD patients were first described by the German neuropsychiatrist Alois Alzheimer in 1906 during the post-mortem examination of a mentally ill patient whose deterioration he had observed until her death. The lesions consisted of dense extracellular deposits, now designated as neuritic or senile plaques, and intracellular dense bundles of fibrils, which are now known as neurofibrillary tangles. Currently, diagnosis of AD with adequate testing is approximately 90% accurate. It

AMYLOID β-PROTEIN (1-42)
Cleavage of amyloid precursor protein (APP) by β- and γ-secretases yields amyloid β peptides. Aβ 1-40 and the more virulent Aβ 1-42 are the most important APP degradation products. Aβ42 is the main constituent of amyloid plaques.
is based on the exclusion of a variety of diseases causing similar symptoms and a careful neurological and psychiatric examination, as well as neuropsychological testing. Imaging technologies for detecting amyloid plaques and tangles in vivo are becoming more precise and thus a valuable additional tool. Numerous potential biomarkers as α1-antitrypsin, complement factor H, α2-macroglobulin, apolipoprotein J, and apolipoprotein A-I for diagnosing AD are being evaluated. However, post-mortem histopathological examination of the brain is still the only definite diagnosis of this disease.

AD can be either inherited or sporadic. The inherited or familial AD is rare and comprises only 5–10% of all cases. Autosomal dominant mutations in the amyloid β/A4 protein precursor (APP) gene on chromosome 21 and the presenilin-1 or -2 genes on chromosomes 14 and 1, respectively, have been attributed to the early onset (before the age of 65) of this disease. APP belongs to the type-1 integral membrane glycoproteins with at least 10 isoforms generated by alternative splicing of the 19 exons. The predominant transcripts are APP695, APP751, and APP770. A number of mutations within the APP gene have been detected in families with an inherited risk for early onset of AD. Usually, they are named after the region, in which they have been detected, e.g. the London APP717 mutations (V717I, V717F, V717G), the Swedish APP670/671 double mutation (K670N/M671L), the Flemish APP692 mutation (A692G), or the Dutch APP693 mutation (E693Q). The Swedish mutation of the β-secretase cleavage site of APP and mutations of positions 692–694 (Aβ 21-23), which strongly influence the aggregation behavior of Aβ, have been studied extensively.

A choice of relevant mutations in the Aβ region of APP is assembled in the table on page 3. The presenilins are another group of proteins involved in the development of AD. Presenilins are integral membrane proteins with eight transmembrane domains localized in the endoplasmic reticulum and the Golgi apparatus. A multitude of mutations within the presenilin-1 and two within the presenilin-2 gene account for most of the cases of early onset of AD.

Genetic factors may contribute as well to the late onset of AD. Increased susceptibility is associated with the expression of different apolipoprotein E (ApoE) isoforms due to the polymorphism in the APOE gene on chromosome 19. In the central nervous system, ApoE has been implicated in growth and repair during development or after injury. Carriers of the APOEε4 allele show a higher risk in developing the disease than carriers of the other two possible alleles APOEε2 and APOEε3. The ApoEε4 effect seems to be dose-dependent since individuals with two of these alleles seem to be at two-fold higher risk to develop the disease than those with one allele. Polymorphisms of the α2-macroglobulin gene on chromosome 12 and the gene coding low-density lipoprotein receptor-related protein 1 (LRP-
Amyloid Peptides

AD THERAPEUTIC STRATEGIES RELY ON DETAILED KNOWLEDGE OF THE MOLECULES INVOLVED

1), LRP1-C/T, have also been suggested to be a risk factor for the late onset of AD. However, further studies in this field are required.

A number of additional, most diverse risk factors have been proposed. These include gender, ethnic group, head trauma, cardiovascular diseases, and educational level. Women, Hispanics, individuals who have experienced a head trauma earlier in life, and persons who suffer from cardiovascular diseases appear to have a higher risk of developing the disease.

The etiology of AD is still not completely understood. Initial research focused upon determining the molecular structure of the senile plaques and the neurofibrillary tangles originally described by Alois Alzheimer. The main constituents of the senile plaques were identified as cleavage products of APP, designated as amyloid β-peptides (Aβ peptides). Depending on the composition and the fraction of fibrillar to non-fibrillar forms of these amyloid peptides, several kinds of senile plaques can be distinguished. Three types of proteases, α-secretase, β-secretase (or β-site APP-cleaving enzyme, BACE), and γ-secretase are involved in APP processing. APP can either be processed by the α- and γ- or by the β- and γ-secretases. The major two amyloid peptides identified in senile plaques, amyloid β-protein (1-40) (Aβ40) and amyloid β-protein (1-42) (Aβ42), are generated by successive proteolysis of APP by β- and γ-secretases. Cleavage of APP by β-secretase results in the release of the extracellular N-terminal protein fragment known as soluble APP-β molecule (sAPP-β). Then, the membrane-retained APP is further processed within the transmembrane domain by γ-secretase to yield either Aβ40 or Aβ42. The formation of Aβ40 and Aβ42 is a normal process, and both peptides can be detected in the plasma and cerebrospinal fluid (CSF) of healthy subjects. In most studies, similar concentrations of Aβ40 have been measured in the CSF of both healthy controls and AD patients. On the other hand, Aβ42 concentrations in the CSF of AD patients are significantly lower than in normal controls, probably reflecting an increased deposition as insoluble plaques.

The neurofibrillary tangles found inside neurons of Alzheimer’s brains are composed of paired helical filaments whose main components are hyperphosphorylated forms of tau, a microtubule associated protein involved in promoting microtubule assembly and stabilization. Self-assembly into paired helical filaments is believed to be a result of hyperphosphorylation due to either the increased activity of protein kinases or the decreased activity of phosphatases.

Several lines of evidence support the view that the accumulation of Aβ42 in the brain is a primary event in the development of AD. Increased cerebral Aβ production appears to be characteristic for all the mutations within the APP and the presenilin genes of familial AD. In patients with Down syndrome (trisomy 21), elevated levels of APP and Aβ due to a third copy of the APP gene result in deposition of Aβ at an early age between 20 and 30.
Formation of neurofibrillary tangles is considered as a consequence of Aβ deposition with a further impact on the progression of the disease possibly due to disruption of axonal transport mechanisms in neurons.

The detailed knowledge about the molecules involved in AD has led to the development of several therapeutic strategies. One strategy aims at the reduction of Aβ40 and Aβ42 by inhibition of either β- or γ-secretase activity or by clearance of Aβ in the brain by means of immunization with these peptides. Transition metals as Cu, Fe and Zn play an important role in the pathology of AD. Aggregation and neurotoxicity of Aβ are dependent on the presence of copper, so Cu-chelating agents showed promising effects in animal models. Another approach is the prevention of the cellular inflammatory response in the cerebral cortex elicited by the progressive accumulation of Aβ. Further preventive therapeutic strategies are based on the findings that cholesterol lowering drugs such as statins and estrogen replacement therapy reduce the risk of developing AD. An additional treatment alternative would be the inhibition of the serine-threonine protein kinases, glycogen synthase kinase 3 (GSK-3) and cyclin-dependent kinase 5 (CDK5), which are probably responsible for the phosphorylation of the tau protein. Inhibition of calpain, an enzyme showing increased activity in AD brains, led to promising results in animal studies. Calpain cleaves the CDK5 activator p35 leading to p25 formation and CDK5 overactivation. Several acetylcholinesterase inhibitors such as tacrine, donepezil, rivastigmine, and galantamine have been approved for the treatment of mild to moderate AD by the FDA. They act by reducing the deficits of the neurotransmitter acetylcholine associated with cognitive impairment in AD patients. The amantadine derivative memantine, an NMDA receptor antagonist, which was already used for the treatment of moderate to severe AD in Europe, has also gained approval in the United States by the FDA. Despite the many promising therapeutic approaches, AD still remains a major burden for the patients, their relatives, and the society.
REFERENCES

P.M. Gorman and A. Chakrabartty

T. Hartmann

P.L. McGeer and E.G. McGeer

D.J. Selkoe

R. Cacabelos

J. Hardy and D.J. Selkoe

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K. Irie et al.

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A.K. Tickler et al.

P. Westermark

E. Levy et al.

K. Takano et al.

T. Tomita and T. Iwatsubo

Y. J. Wang et al.

J.X. Chen and S.D. Yan

M.A. Findeis

V.H. Finder and R. Glockshuber

M. Li et al.

P. Westermark
Aspects on human amyloid forms and their fibril polypeptides. FEBS J. 272, 5942-5949 (2005)

E. Levy et al.
Studies on the first described Alzheimer’s disease amyloid beta mutant, the Dutch variant. J. Alzheimers Dis. 9, 329-339 (2006)

K. Takano et al.

B. Van Broeck et al.

L.B. Hersh and D.W. Rogers

REFERENCES

P.M. Gorman and A. Chakrabartty

T. Hartmann

P.L. McGeer and E.G. McGeer

D.J. Selkoe

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K. Irie et al.

M.R. Nichols et al.

E.M. Sigurdsson

A.K. Tickler et al.

P. Westermark

E. Levy et al.

K. Takano et al.
Y. Ohyagi
Intracellular amyloid beta-protein as a therapeutic target for treating Alzheimer’s disease.

K.A. Bates et al.
Clearance mechanisms of Alzheimer’s amyloid-beta peptide: implications for therapeutic design and diagnostic tests.

R. Deane et al.
Clearance of amyloid-beta peptide across the blood-brain barrier: implication for therapies in Alzheimer’s disease.

F. Song et al.
Plasma biomarkers for mild cognitive impairment and Alzheimer’s disease.
Brain Res. Rev. 61, 69-80 (2009) Review

E. Bruno et al.
Lack of interaction between LRP1 and A2M polymorphisms for the risk of Alzheimer disease.

H.J. Garringer et al.
Modeling familial British and Danish dementia.

A. Kitamura and H. Kubota
Amyloid oligomers: dynamics and toxicity in the cytosol and nucleus.

B. Liang et al.
Calpain activation promotes BACE1 expression, amyloid precursor protein processing, and amyloid plaque formation in a transgenic mouse model of Alzheimer disease.

C.J. Lin et al.
Cu(II) interaction with amyloid-beta peptide: a review of neuroactive mechanisms in AD brains.

M.L. Moro et al.
Alzheimer’s disease and amyloid beta-peptide deposition in the brain: a matter of ‘aging’?

K. Murakami et al.
The turn formation at positions 22 and 23 in the 42-mer amyloid beta peptide: the emerging role in the pathogenesis of Alzheimer’s disease.

M.P. Murphy and H. LeVine 3rd
Alzheimer’s disease and the amyloid-beta peptide.

J.F. Quinn et al.
A copper-lowering strategy attenuates amyloid pathology in a transgenic mouse model of Alzheimer’s disease.
J. Alzheimers Dis. 21, 903-914 (2010)

D.R. Thal et al.
Capillary cerebral amyloid angiopathy identifies a distinct APOE epsilon4-associated subtype of sporadic Alzheimer’s disease.
Acta Neuropathol. 120, 169-183 (2010)

N. Venketasubramanian et al.
Interethnic differences in dementia epidemiology: global and Asia-Pacific perspectives.
Bachem’s offer for Alzheimer’s research comprises a broad choice of amyloid peptide fragments including Aβ mutant peptides.

For more details on our Alzheimer’s disease peptides, please go to: shop.bachem.com
AMYLOID β-PROTEIN (1-42)

Amyloid β-Protein (1-42)
H-1368
DAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGLMVGGVIA

Amyloid β-Protein (1-42) (Hydrochloride salt)
H-6466
DAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGLMVGGVIA
(Hydrochloride salt)

ent-Amyloid β-Protein (1-42)
H-5566
daefrhdsgyevhhqklffaedvgsnkgaiglmvgvvia
(all-D peptide)

Amyloid β-Protein (42-1)
H-3976
AIVVGGVMLGIIAGKNSGVDEAFFVLKH-VHEY

Amyloid β-Protein (1-42) (mouse, rat)
H-5966
DAEFRHDGFEVRHQKLFFAEDVGSNK-GAIIGLMVGGVIA

(Arg¹⁷)-Amyloid β-Protein (1-42)
H-6448
DAEFRHDSGYEVHHQKRFFAEDVGSNK-GAIIGLMVGGVIA

(D-Asp¹)-Amyloid β-Protein (1-42)
H-4854
dAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGLMVGGVIA

Biotinyl-Amyloid β-Protein (1-42)
H-5642
Biotinyl-DAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGLMVGGVIA

Cys-Gly-Lys-Arg-Amyloid β-Protein (1-42)
H-6388
CGKRDAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGLMVGGVIA

FITC-β-Ala-Amyloid β-Protein (1-42)
M-2585
FITC-β-Ala-DAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGLMVGGVIA

(Glu²⁰)-Amyloid β-Protein (1-42)
H-6446
DAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGLMVGGVIA

(Gly²²)-Amyloid β-Protein (1-42)
H-6124
DAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGLMVGGVIA
(Arctic Mutation E22G)

(Met(O)³⁵)-Amyloid β-Protein (1-42)
H-5888
DAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGLMVGGVIA

(Met(O₂)³⁵)-Amyloid β-Protein (1-42)
H-7324
DAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGLMVGGVIA

(Nle³⁵)-Amyloid β-Protein (1-42)
H-7308
DAEFRHDSGYEVHHQKLFFAEDVGSNK-GAIIGL-Nle-VGGVIA
AMYLOID β-PROTEIN (1-40)

Amyloid β-Protein (1-40) (Trifluoroacetate salt)
H-1194
DAEFRHSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV
(Trifluoroacetate salt)

Amyloid β-Protein (1-40) (Hydrochloride salt)
H-5568
DAEFRHSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV
(Hydrochloride salt)

Amyloid β-Protein (40-1)
H-2972
VVGVMLGIIAGKNSGVDEAFFVLKQHH-VEYGDHRFEAD

Amyloid β-Protein (1-40) (mouse, rat)
H-5638
DAEFGHSGFEVRHQKLVFFAEDVGSNK-GAIIGLMVGGVV

(Arg3)-Amyloid β-Protein (1-40)
H-6432
DAEFRHDSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV
(English Mutation H6R)

(Arg5)-Amyloid β-Protein (1-40)
H-7336
DAEFRHDSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV
(Tottori Mutation D7N)

(Asn7)-Amyloid β-Protein (1-40)
H-7334
DAEFRHNSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV
(Italian Mutation E22K)

(Asn23)-Amyloid β-Protein (1-40)
H-7332
DAEFRHDSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV
(Iowa Mutation D23N)

(Asn(4-aminobutyl)1-22,Gln(4-aminobutyl)9-11-22)-Amyloid β-Protein (1-40)
H-4984
N(4-aminobutyl)AQ(4-aminobutyl)FRHN(4-aminobutyl)SGYQ(4-aminobutyl)VHHQKLVFFAQ(4-aminobutyl)N(4-aminobutyl)VGSNKGAIIGLMVGGVV

Biotinyl-Amyloid β-Protein (1-40)
H-5914
Biotinyl-DAEFRHDSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV

(Cys5)-Amyloid β-Protein (1-40)
H-7368
CDAEFRHDSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV

(7-Diethylaminocoumarin-3-yl)carbonyl-Amyloid β-Protein (1-40)
H-6468
Deac-DAEFRHDSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV

FITC-β-Ala-Amyloid β-Protein (1-40)
H-6326
FITC-β-Ala-DAEFRHDSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV

(Gln9)-Amyloid β-Protein (1-40)
H-6434
DAEFRHDSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV
(Dutch Mutation E22Q)

(Gly21)-Amyloid β-Protein (1-40)
H-6694
DAEFRHDSGYEVHHQKLVFFAGDVGSNK-GAIIGLMVGGVV
(Flemish Mutation A21G)

(Gly22)-Amyloid β-Protein (1-40)
H-6696
DAEFRHDSGYEVHHQKLVFFAEDVGSNK-GAIIGLMVGGVV

(Lys22)-Amyloid β-Protein (1-40)
H-6698
DAEFRHDSGYEVHHQKLVFFAGDVGSNK-GAIIGLMVGGVV
(Italian Mutation E22K)
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<th>Acetyl-Amyloid β-Protein (15-20) amide</th>
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AMYLOID β-PROTEIN FRAGMENTS (CONTINUED)

(Arg¹⁵,Asp¹⁸-²⁵,Pro¹⁸-²¹-²³,Val²²,Ile²⁴)-Amyloid β-Protein (15-25)
H-3904
RDLPFFPVPID

Gly-Amyloid β-Protein (15-25)-Gly-ε-aminocaproyl(−Lys)₆
H-3978
GQKLVFAEDYGG-εAhx-KKKKKK

H-Leu-Leu-Val-Phe-OH
(Leu¹⁶)-Amyloid β-Protein (16-19)
H-3945
LLVF

tent-[Amyloid β-Protein (20-16)]-β-Ala-D-Lys(tent-[Amyloid β-Protein (16-20)])
H-6074
ffvlk-β-Ala-k(ffvlk)

Amyloid β-Protein (16-20)
H-3682
KLVFF

(Pro¹⁸,Asp²¹)-Amyloid β-Protein (17-21)
H-4876
LPFFD

Acetyl-(Pro¹⁸,Asp²¹)-Amyloid β-Protein (17-21) amide
H-6138
Ac-LPFFD-NH₂

Amyloid β-Protein (20-29)
H-3808
FAEDVGSKNG

Amyloid β-Protein (22-35)
H-1976
EDVGSNKGAIGLM

Amyloid β-Protein (29-40)
H-3984
GAIGLVMGGVV

Propionyl-Amyloid β-Protein (31-34) amide
H-4124
Propionyl-IIIGL-NH₂

Amyloid β-Protein (31-35)
H-5866
IIGLM

Cys-Gly-His-Gly-Asn-Lys-Ser-Amyloid β-Protein (33-40)
H-6364
CGHGNKSLMVGGVV

Cys-Gly-Lys-Lys-Gly-Amyloid β-Protein (33-40)
H-6372
CGKKGLMVGGVV

Amyloid β-Protein (33-42)
H-5572
GLMVGGVVIA

Cys-Gly-Lys-Lys-Gly-Amyloid β-Protein (35-40)
H-6376
CGKKGMVGGVV

Cys-Gly-Lys-Lys-Gly-Amyloid β-Protein (36-42)
H-6378
CGKKGVGGVVIA

H-Val-Gly-Gly-OH
(Amyloid β-Protein (36-38))
H-5270
VGG

H-Gly-Gly-Val-OH
(Amyloid β-Protein (37-39))
H-3500
GGV

Methoxysuccinyl-Val-Val-Ile-Ala-pNA
(Methoxysuccinyl-Amyloid β-Protein (39-42)-p-nitroanilide)
L-1745
MeOSuc-VVIA-pNA
AMYLOID β/A4 PROTEIN PRECURSOR (APP) FRAGMENTS

Acetyl-Amyloid β/A4 Protein Precursor\textsubscript{770} (96-110) (cyclized)  
H-2232  
Ac-NWCKRGRKQCKTPH-NH\textsubscript{2}  
(Disulfide bond)

Amyloid β/A4 Protein Precursor\textsubscript{770} (135-155)  
H-3726  
FLHQERMDVCEHLHWHTVAK

Amyloid β/A4 Protein Precursor\textsubscript{770} (394-410)  
H-2594  
AKERLEAKHRERMSQVM

Amyloid β/A4 Protein Precursor\textsubscript{770} (403-407)  
H-1608  
RERMS

Amyloid β/A4 Protein Precursor\textsubscript{770} (586-595)  
(human, mouse, rat)  
N-1850  
ISYGNDALMP

Amyloid β/A4 Protein Precursor\textsubscript{770} (667-675)  
H-4836  
SEVNLDAEFR  
(Swedish Double Mutation K670N / M671L)

Amyloid β/A4 Protein Precursor\textsubscript{770} (667-676)  
H-4834  
SEVNLDÆFR  
(Swedish Double Mutation K670N / M671L)

Amyloid β/A4 Protein Precursor\textsubscript{770} (667-676)  
H-4838  
SEVKVDAEFR

Amyloid β/A4 Protein Precursor\textsubscript{770} (740-770)  
H-6216  
AAVTPEERHLSKMQNGY-ENPTYKFFEQMQN

AMYLOID-LIKE PROTEIN

APL\textsubscript{1825}  
H-7302  
DELAPAGTGVSVRVEAVSLLIMGAGG

APL\textsubscript{1827}  
H-7304  
DELAPAGTGVSVRVEAVSLLIMGAGGS

APL\textsubscript{1828}  
H-7306  
DELAPAGTGVSVRVEAVSLLIMGAGG-GL
AMYLOID BRI PEPTIDES

**Amyloid Bri Protein (1-23)**
- H-5052
- EASNCFAIRHFENKFAVETLICS
  (Disulfide bond)

**Amyloid Bri Protein (1-34)**
- H-5526
- <EASNCFAIRHFENKFAVETLICSRT-VKKNIIEEN>
  (Disulfide bond)

**Amyloid Bri Protein (1-34) (reduced)**
- H-4728
- <EASNCFAIRHFENKFAVETLICSRT-VKKNIIEEN>

**Amyloid Bri Protein Precursor**
- 277 (89-106)
- H-5048
- CGIYIKDDVILNEPSAD

AMYLOID DAN PEPTIDES

**Amyloid Dan Protein (1-34)**
- H-5528
- <EASNCFAIRHFENKFAVETLICFNL-FLNSQEKHY>
  (Disulfide bond)

**Amyloid Dan Protein (1-34) (reduced)**
- H-5298
- <EASNCFAIRHFENKFAVETLICFNL-FLNSQEKHY>

AMYLOID P-COMPONENT PEPTIDES

**Amyloid P Component (27-38) amide**
- H-2942
- EKPLQNFTLCFR-NH₂

**Tyr-Amyloid P Component (27-38) amide**
- H-2944
- YEKPLQNFTLCFR-NH₂

**Amyloid P Component (33-38) amide**
- H-2946
- FTLCFR-NH₂

NON-Aβ COMPONENT

**Non-Aβ Component of Alzheimer’s Disease**
(α-Synuclein (61-95) (human))
- H-2598
- EQVTNVGGAVVTGVTAVAQKTVEGAG-SIAAATGFV
Inhibitors and substrates for β- and γ-secretase and further peptides and biochemicals for Alzheimer’s research are available on our online shop at shop.bachem.com:

- Areas of Interest
  - Alzheimer’s Disease
**AMYLOID PEPTIDES**

**β-SECRETASE SUBSTRATES**

DABCYL-(Asn<sub>670</sub>,Leu<sub>671</sub>)-Amyloid β/A4 Protein Precursor<sub>770</sub> (661-675)-EDANS  
M-2445  
DABCYL-IKTEEISEVNLDAEF-EDANS

H-Lys-Thr-Glu-Glu-Ile-Ser-Glu-Val-Lys-Met-pNA  
(APP<sub>770</sub> (662-671)-pNA)  
L-1905  
KTEEISEVKM-pNA

Mca-(Asn<sub>670</sub>,Leu<sub>671</sub>)-Amyloid β/A4 Protein Precursor<sub>770</sub> (667-674)-Dap(Dnp)  
M-2425  
Mca-SEVNLDAE-Dpa

DABCYL-(Asn<sub>670</sub>,Leu<sub>671</sub>)-Amyloid β/A4 Protein Precursor<sub>770</sub> (667-675)-EDANS  
M-2435  
DABCYL-SEVNLDAEF-EDANS

Mca-(Asn<sub>670</sub>,Leu<sub>671</sub>)-Amyloid β/A4 Protein Precursor<sub>770</sub> (667-675)-Lys(Dnp)  
M-2420  
Mca-SEVNLDAEFK(Dnp)

Mca-(Asn<sub>670</sub>,Leu<sub>671</sub>)-Amyloid β/A4 Protein Precursor<sub>770</sub> (667-675)-Lys(Dnp) amide  
M-2485  
Mca-SEVNLDAEFK(Dnp)-NH₂

Lys(Dabsyl)-(Asn<sub>670</sub>,Leu<sub>671</sub>)-Amyloid β/A4 Protein Precursor<sub>770</sub> (667-676)-Gln-Lucifer Yellow  
M-2570  
K(Dabsyl)SEVNLDAAEFRQ-Lucifer Yellow

Mca-Amyloid β/A4 Protein Precursor<sub>770</sub> (667-676)-Lys(Dnp)-Arg-Arg amide  
M-2460  
Mca-SEVKMDAEFRK(Dnp)RR-NH₂
**β-SECRETASE INHIBITORS**

- Ac-Val-Met-[(2S,4S,5S)-5-amino-4-hydroxy-2-isopropyl-7-methyl-octanoyl]-Ala-Glu-Phe-OH  
  **N-1815**  
  Ac-VML-psi[CHOHCH₂]VAEF

- (Asn⁶⁷⁰, Sta⁶⁷¹, Val⁶⁷²)-Amyloid β/A4 Protein Precursor₇₇₀ (662-675)  
  **H-4848**  
  KTEEESEQN-Sta-VAEF

- H-Glu-Leu-Asp-[(2R,4S,5S)-5-amino-4-hydroxy-2,7-dimethyl-octanoyl]-Ala-Glu-Phe-OH  
  **N-1825**  
  ELDL-psi[CHOHCH₂]AAEF

  **N-1920**  
  ELDL-psi[CHOHCH₂]AAEF

- Om99-2  
  **H-5108**  
  EVNL-psi[CHOHCH₂]AAEF

- Z-Leu-Leu-4,5-dehydro-Leu-aldehyde  
  **N-1590**  
  Z-LLΔL-CHO

**γ-SECRETASE SUBSTRATES**

- Abz-Amyloid β/A4 Protein Precursor₇₇₀ (708-715)-Lys(Dnp)-D-Arg-D-Arg-D-Arg amide  
  **M-2540**  
  Abz-GGVVIATVK(Dnp)rrr-NH₂

- N-Me-Abz-Amyloid β/A4 Protein Precursor₇₇₀ (708-715)-Lys(Dnp)-D-Arg-D-Arg-D-Arg amide  
  **M-2555**  
  N-Me-Abz-GGVVIATVK(Dnp)rrr-NH₂

**γ-SECRETASE INHIBITORS**

- L-685,458  
  **H-5106**  
  Boc-F-psi[CHOHCH₂]FLF-NH₂

- 3,5-Difluorophenylacetyl-Ala-Phg-OMe  
  **N-1890**

- Z-Ile-Leu-aldehyde  
  **N-1895**  
  Z-IL-CHO

- Z-Leu-Leu-Nle-aldehyde  
  **N-1695**  
  Z-LL-Nle-CHO
**HUMANIN**

Colivelin  
H-6336  
SALLRSIPAPAGASRLLLLTGEIDLPLP

(Gly^{14})-Humanin (human)  
H-5576  
MAPRGFSCLLLLTGEIDLPVKRA

Humanin (human)  
H-5574  
MAPRGFSCLLLLTSEIDLPVKRA

**VARIOUS RELATED PRODUCTS**

(trans, trans)-1-Bromo-2,5-bis-(3-carboxy-4-hydroxy)styrylbenzene (BSB)  
Q-2690

L-Carnosine  
G-1250

CRF (6-33) (human, rat)  
H-3456  
ISLDLTFLLLREVLEMAREQLAQA-HS

H-D-Pen-OH  
(D-Penicillamine)  
F-4235

Phenserine  
Q-1860

Presenilin-1 (331-349)-Cys (human, mouse)  
H-3988  
NDDGGFSEEEWAFRSDHLGC

Z-Val-Lys-Met-AMC  
I-1625  
Z-VKM-AMC
ALZHEIMER CELL CULTURE, SEM

Coloured SEM of Alzheimer’s disease culture cells.

Alzheimer’s disease culture cells. Coloured scanning electron micrograph (SEM) of cells used in Alzheimer’s disease research. These cells have been genetically engineered to produce amyloid precursor protein (APP), which in turn forms the protein amyloid. Plaques of amyloid in the brain are a major pathological feature of Alzheimer’s disease. These cells are cultured from a nerve cancer (neuroblastoma), and have shorter and more numerous processes (dendrites and axons) than healthy nerve cells. Alzheimer’s is a brain-wasting disease common in the elderly. It causes confusion, memory loss, personality changes and eventually death.

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