Amyloid Beta 40-S26C Monomer and Dimer

Soluble amyloid ß-protein dimers isolated from Alzheimer cortex directly induce Tau hyperphosphorylation and neuritic degeneration

Amyloid-beta protein dimers isolated directly from Alzheimer's brains impair synaptic plasticity and memory.

Alzheimer's disease constitutes a rising threat to public health. Despite extensive research in cellular and animal models, identifying the pathogenic agent present in the human brain and showing that it confers key features of Alzheimer's disease has not been achieved. We extracted soluble amyloid-beta protein (Abeta) oligomers directly from the cerebral cortex of subjects with Alzheimer's disease. The oligomers potently inhibited long-term potentiation (LTP), enhanced long-term depression (LTD) and reduced dendritic spine density in normal rodent hippocampus. Soluble Abeta from Alzheimer's disease brain also disrupted the memory of a learned behavior in normal rats. These various effects were specifically attributable to Abeta dimers. Mechanistically, metabotropic glutamate receptors were required for the LTD enhancement, and N-methyl D-aspartate receptors were required for the spine loss. Co-administering antibodies to the Abeta N-terminus prevented the LTP and LTD deficits, whereas antibodies to the midregion or C-terminus were less effective. Insoluble amyloid plaque cores from Alzheimer's disease cortex did not impair LTP unless they were first solubilized to release Abeta dimers, suggesting that plaque cores are largely inactive but sequester Abeta dimers that are synaptotoxic. We conclude that soluble Abeta oligomers extracted from Alzheimer's disease brains potently impair synapse structure and function and that dimers are the smallest synaptotoxic species.

Shankar et al, Nat Med. 2008 Aug;14(8):837-42. Epub 2008 Jun 22.

Soluble amyloid beta-protein dimers isolated from Alzheimer cortex directly induce Tau hyperphosphorylation and neuritic degeneration.

Alzheimer disease is a major cause of cognitive failure, and a pathogenically related but more subtle process accounts for many cases of mild memory symptoms in older humans. Insoluble fibrillar plaques of amyloid ß-proteins (Aß) and neurofibrillary deposits of hyperphosphorylated tau proteins are the diagnostic lesions of AD, but their temporal mechanistic relationship has long been debated. The recent recognition that small, diffusible oligomers may be the principal bioactive form of Aß raises the key question of whether these are sufficient to initiate cytoskeletal change and neurite degeneration. A few studies have examined the effects of oligomers of synthetic Aß peptides of one defined length at supraphysiological concentrations, but the existence of such assemblies in the AD brain is not established. Here, we isolated Aß dimers, the most abundant form of soluble oligomer detectable in the human brain, from the cortices of typical AD subjects and found that at subnanomolar concentrations, they first induced hyperphosphorylation of tau at AD-relevant epitopes in hippocampal neurons and then disrupted the microtubule cytoskeleton and caused neuritic degeneration, all in the absence of amyloid fibrils. Application of pure, synthetic dimers confirmed the effects of the natural AD dimers, although the former were far less potent. Knocking down endogenous tau fully prevented the neuritic changes, whereas overexpressing human tau accelerated them. Coadministering Aß N-terminal antibodies neutralized the cytoskeletal disruption. We conclude that natural dimers isolated from the AD brain are sufficient to potently induce AD-type tau phosphorylation and then neuritic dystrophy, but passive immunotherapy mitigates this.

Jin, et al: Proc Natl Acad Sci U S A. 2011 Apr 5;108(14):5819-24. Epub 2011 Mar 18.

PHOENIX PHARMACEUTICALS, INC.
330 BEACH ROAD, BURLINGAME CA, 94010, USA
PHONE: **(650) 558-8898** EMAIL: **info@phoenixpeptide.com**
WWW.PHOENIXPEPTIDE.COM

PHOENIX EUROPE GMBH
VIKTORIASTRASSE 3-5, D-76133 KARLSRUHE, GERMANY
PHONE: **+49-721-1611950** EMAIL: **germany@phoenixpeptide.com**
WWW.PHOENIXPEPTIDE.COM

A Beta 40-S26C Monomer and Dimer

Catalog No.	Product Name	Standard Size
018-71	Amyloid beta 40-S26C dimer (Human)	100ug
018-73	Amyloid beta 40-S26C monomer (Human)	100ug

Other Beta-Amyloid Products

Catalog No.	Product Name	Standard Size
018-23	Amyloid beta (17-42) (Human)	100 µg
018-24	Amyloid beta (9-42) (Human)	100 µg
018-71	Amyloid beta 40-S26C dimer (Human)	100ug
018-73	Amyloid beta 40-S26C monomer (Human)	100ug
018-02	Amyloid beta-Protein (1-28) / Alzheimer's Disease beta-Protein / SP-28 (Human)	200 µg
018-01	Amyloid beta-Protein (1-40) (Human)	200 µg
H-018-01	Amyloid beta-Protein (1-40) (Human) - Antibody for Immunohistochemistry	50 µl
FC3-018-01	Amyloid beta-Protein (1-40) (Human) - Cy3 Labeled	1 nmol
FC5-018-01	Amyloid beta-Protein (1-40) (Human) - Cy5 Labeled	1 nmol
T-018-01	Amyloid beta-Protein (1-40) (Human) - I-125 Labeled	10 µCi
T-G-018-01	Amyloid beta-Protein (1-40) (Human) - I-125 Labeled Purified IgG	10 µCi
G-018-01	Amyloid beta-Protein (1-40) (Human) - Purified IgG Antibody	400 µg
018-07	Amyloid beta-Protein (1-42) (Human)	200 µg
T-018-07	Amyloid beta-Protein (1-42) (Human) - I-125 Labeled	10 µCi
018-06	Amyloid beta-Protein (1-43) (Human)	200 µg
018-08	Amyloid beta-Protein (10-20) (Human)	500 µg
018-04	Amyloid beta-Protein (12-28) / Alzheimer's Disease beta-Protein / SP-17 (Human)	200 µg
018-05	Amyloid beta-Protein (25-35) (Human)	200 µg
018-09	Amyloid beta-Protein / A4-Protein Precursor (328-332)	1 mg
018-03	Amyloid beta-Protein [Gln11] (1-28) / Alzheimer's Disease beta-Protein / SP-28 (Human)	200 µg
018-63	Amyloid Beta-Protein, [pGlu11] (11-42) (Human)	100µg
018-64	Amyloid Beta-Protein, [pGlu3] (3-42) (human)	100 µg
025-43	Amyloid P Component (27-38) Amide / SAP-1 (Human)	500 µg
018-70	APP Intracellular Domain (AICD Long Form) / Beta-Amyloid Precursor (712-770) (Human)	100 ug
B-018-70	APP Intracellular Domain (AICD Long Form) / Beta-Amyloid Precursor (712-770) (Human) - Biotin Labeled	20 µg
T-018-70	APP Intracellular Domain (AICD Long Form) / Beta-Amyloid Precursor (712-770) (Human) - I-125 Labeled	10 µCi
018-69	APP Intracellular Domain (AICD Short Form) / Beta-Amyloid Precursor (727-770) (Human)	100 µg
B-018-69	APP Intracellular Domain (AICD Short Form) / Beta-Amyloid Precursor (727-770) (Human) - Biotin Labeled	20 µg
T-018-69	APP Intracellular Domain (AICD Short Form) / Beta-Amyloid Precursor (727-770) (Human) - I-125 Labeled	10 µCi
018-65	Beta-Amyloid Precursor (430-467) (Human)	100 µg
B-018-65	Beta-Amyloid Precursor (430-467) (Human) - Biotin Labeled	20 µg
T-018-65	Beta-Amyloid Precursor (430-467) (Human) - I-125 Labeled	10 µCi
018-66	Beta-Amyloid Precursor (471-494) (Human)	100 µg
B-018-66	Beta-Amyloid Precursor (471-494) (Human) - Biotin Labeled	20 µg
T-018-66	Beta-Amyloid Precursor (471-494) (Human) - I-125 Labeled	10 µCi
018-67	Beta-Amyloid Precursor (497-520) (Human)	100 µg
B-018-67	Beta-Amyloid Precursor (497-520) (Human) - Biotin Labeled	20 µg
T-018-67	Beta-Amyloid Precursor (497-520) (Human) - I-125 Labeled	10 µCi
018-68	Beta-Amyloid Precursor (740-770) / C-31 (Human)	100 µg
B-018-68	Beta-Amyloid Precursor (740-770) / C-31 (Human) - Biotin Labeled	20 µg
T-018-68	Beta-Amyloid Precursor (740-770) / C-31 (Human) - I-125 Labeled	10 µCi