Alzheimer's Disease Related Peptides

Short Form of APP Intracellular Domain (AICD) (Human) = Human Beta-Amyloid Precursor (727-770), Catalog No.: 018-69

Long Form of APP Intracellular Domain (AICD) (Human) = Human Beta-Amyloid Precursor (712-770), Catalog No.: 018-70

APP Intracellular Domain (AICD) Contributes to AD Pathology Independently of A-beta

Alzheimer's disease-like pathological features in transgenic mice expressing the APP intracellular domain

The hypothesis that amyloid-beta (ABeta) peptides are the primary cause of Alzheimer's disease (AD) remains the best supported theory of AD pathogenesis. Yet, many observations are inconsistent with the hypothesis. ABeta peptides are generated when amyloid precursor protein (APP) is cleaved by presenilins, a process that also produces APP intracellular domain (AICD). We previously generated AICD-overexpressing transgenic mice that showed abnormal activation of GSK-3Beta, a pathological feature of AD. We now report that these mice exhibit additional AD-like characteristics, including hyperphosphorylation and aggregation of tau, neurodegeneration and working memory deficits that are prevented by treatment with lithium, a GSK-3Beta inhibitor. Consistent with its potential role in AD pathogenesis, we find AICD levels to be elevated in brains from AD patients. The in vivo findings that AICD can contribute to AD pathology independently of ABeta have important therapeutic implications and may explain some observations that are discordant with the amyloid hypothesis.

Ghosal K., et al. PNAS, 2009,106 (43):18367-18372

ABeta Hinders Nuclear Targeting of AICD and Fe65 in Primary Neuronal Cultures

The intracellular domain of the Alzheimer's amyloid precursor protein (AICD) has been described as an important player in the transactivation of specific genes. It results from proteolytic processing of the Alzheimer's amyloid precursor protein (APP), as does the neurotoxic ABeta peptide. Although normally produced in cells, ABeta is typically considered to be a neurotoxic peptide, causing devastating effects. By exposing primary neuronal cultures to relatively low ABeta concentrations, this peptide was shown to affect APP processing. Our findings indicate that APP C-terminal fragments are increased with concomitant reduction in the expression levels of APP itself. AICD nuclear immunoreactivity detected under control conditions was dramatically reduced in response to ABeta exposure. Additionally, intracellular protein levels of Fe65 and GSK3 were also decreased in response to ABeta. APP nuclear signaling is altered by ABeta, affecting not only AICD production but also its nuclear translocation and complex formation with Fe65. In effect, ABeta can trigger a physiological negative feedback mechanism that modulates its own production. *A. G. Henriques et al. J Mol Neurosci. 2009 September; 39(1-2): 248-255.*

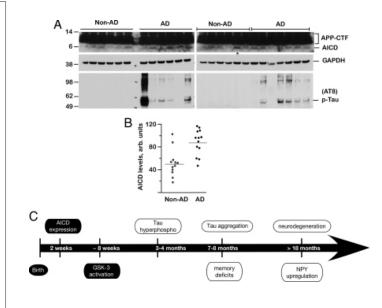


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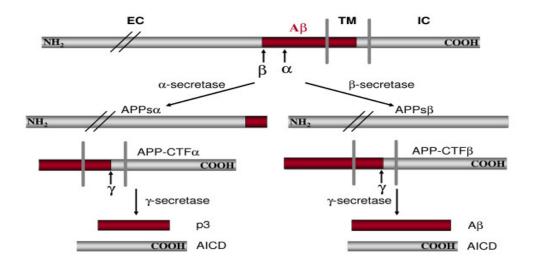
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Human Beta-Amyloid Precursor

MLPGLALLLL AAWTARALEV PTDGNAGLLA	30
EPQIAMFCGR LNMHMNVQNG KWDSDPSGTK	60
TCIDTKEGIL QYCQEVYPEL QITNVVEANQ	90
PVTIQNWCKR GRKQCKTHPH FVIPYRCLVG	120
EFVSDALLVP DKCKFLHQER MDVCETHLHW	150
HTVAKETCSE KSTNLHDYGM LLPCGIDKFR	180
GVEFVCCPLA EESDNVDSAD AEEDDSDVWW	210
GGADTDYADG SEDKVVEVAE EEEVAEVEEE	240
EADDDEDDED GDEVEEEAEE PYEEATERTT	270
SIATTTTTTT ESVEEVVREV CSEQAETGPC	300
RAMISRWYFD VTEGKCAPFF YGGCGGNRNN	330
FDTEEYCMAV CGSAMSQSLL KTTQEPLARD	360
PVKLPTTAAS TPDAVDKYLE TPGDENEHAH	390
FQKAKERLEA KHRERMSQVM REWEEAERQA	420
Beta-Amviold, Prebro (430-467)	
KNLPKADKKA VIQHFQEKVE SLEQEAANER	450
KNLPKADKKA VIQHFQEKVE SLEQEAANER	450 480
KNLPKADKKA VIQHFQEKVE SLEQEAANER	0.0000000
KNLPKADKKA VIQHFQEKVE SLEQEAANER	480
KNLPKADKKA VIQHFQEKVE SLEQEAANER QQLVETHMAR VEAMLNDRRR LALENYITAL Beta-Amyloid, Prepro (471-494) QAVPPRPRHV FNMLKKYVRA EQKDRQHTLK Beta-Amyloid, Prepro (497-520)	480 510
KNLPKADKKA VIQHFQEKVE SLEQEAANER QQLVETHMAR VEAMLNDRRR LALENYITAL Beta-Amyloid, Prepro (471-494) QAVPPRPRHV FNMLKKYVRA EQKDRQHTLK Beta-Amyloid, Prepro (497-520) HFEHVRMVDP KKAAQIRSQV MTHLRVIYER	480 510 540
KNLPKADKKA VIQHFQEKVE SLEQEAANER QQLVETHMAR VEAMLNDRRR LALENYITAL Beta-Amyloid, Prepro (471-494) QAVPPRPRHV FNMLKKYVRA EQKDRQHTLK Beta-Amyloid, Prepro (497-520) HFEHVRMVDP KKAAQIRSQV MTHLRVIYER MNQSLSLLYN VPAVAEEIQD EVDELLQKEQ	480 510 540 570
KNLPKADKKA VIQHFQEKVE SLEQEAANER QQLVETHMAR VEAMLNDRRR LALENYITAL Beta-Amyloid, Prepro (471-494) QAVPPRPRHV FNMLKKYVRA EQKDRQHTLK Beta-Amyloid, Prepro (497-520) HFEHVRMVDP KKAAQIRSQV MTHLRVIYER MNQSLSLLYN VPAVAEEIQD EVDELLQKEQ NYSDDVLANM ISEPRISYGN DALMPSLTET KTTVELLPVN GEFSLDDLQP WHSFGADSVP ANTENEVEPV DARPAADRGL TTRPGSGLTN	480 510 540 570 600
KNLPKADKKA VIQHFQEKVE SLEQEAANER QQLVETHMAR VEAMLNDRRR LALENYITAL Beta-Amyloid, Prepro (471-494) QAVPPRPRHV FNMLKKYVRA EQKDRQHTLK Beta-Amyloid, Prepro (497-520) HFEHVRMVDP KKAAQIRSQV MTHLRVIYER MNQSLSLLYN VPAVAEEIQD EVDELLQKEQ NYSDDVLANM ISEPRISYGN DALMPSLTET KTTVELLPVN GEFSLDDLQP WHSFGADSVP	480 510 540 570 600 630
KNLPKADKKA VIQHFQEKVE SLEQEAANER QQLVETHMAR VEAMLNDRRR LALENYITAL Beta-Amyloid, Prepro (471-494) QAVPPRPRHV FNMLKKYVRA EQKDRQHTLK Beta-Amyloid, Prepro (497-520) HFEHVRMVDP KKAAQIRSQV MTHLRVIYER MNQSLSLLYN VPAVAEEIQD EVDELLQKEQ NYSDDVLANM ISEPRISYGN DALMPSLTET KTTVELLPVN GEFSLDDLQP WHSFGADSVP ANTENEVEPV DARPAADRGL TTRPGSGLTN Beta-Amyloid (1-42) IKTEEISEVK MDAEFRHDSG YEVHHQKLVF FAEDVGSNKG AIIGLMVGGV VIATVIVITL	480 510 540 570 600 630 660
KNLPKADKKA VIQHFQEKVE SLEQEAANER QQLVETHMAR VEAMLNDRRR LALENYITAL Beta-Amyloid, Prepro (471-494) QAVPPRPRHV FNMLKKYVRA EQKDRQHTLK Beta-Amyloid, Prepro (497-520) HFEHVRMVDP KKAAQIRSQV MTHLRVIYER MNQSLSLLYN VPAVAEEIQD EVDELLQKEQ NYSDDVLANM ISEPRISYGN DALMPSLTET KTTVELLPVN GEFSLDDLQP WHSFGADSVP ANTENEVEPV DARPAADRGL TTRPGSGLTN Beta-Amyloid (1-42) IKTEEISEVK MDAEFRHDSG YEVHHQKLVF	480 510 540 570 600 630 660 690
KNLPKADKKA VIQHFQEKVE SLEQEAANER QQLVETHMAR VEAMLNDRRR LALENYITAL Beta-Amyloid, Prepro (471-494) QAVPPRPRHV FNMLKKYVRA EQKDRQHTLK Beta-Amyloid, Prepro (497-520) HFEHVRMVDP KKAAQIRSQV MTHLRVIYER MNQSLSLLYN VPAVAEEIQD EVDELLQKEQ NYSDDVLANM ISEPRISYGN DALMPSLTET KTTVELLPVN GEFSLDDLQP WHSFGADSVP ANTENEVEPV DARPAADRGL TTRPGSGLTN Beta-Amyloid (1-42) IKTEEISEVK MDAEFRHDSG YEVHHQKLVF FAEDVGSNKG AIIGLMVGGV VIATVIVITL Beta-Amyloid, Prepro (727-770)	480 510 540 570 600 630 660 690 720
KNLPKADKKA VIQHFQEKVE SLEQEAANER QQLVETHMAR VEAMLNDRRR LALENYITAL Beta-Amyloid, Prepro (471-494) QAVPPRPRHV FNMLKKYVRA EQKDRQHTLK Beta-Amyloid, Prepro (497-520) HFEHVRMVDP KKAAQIRSQV MTHLRVIYER MNQSLSLLYN VPAVAEEIQD EVDELLQKEQ NYSDDVLANM ISEPRISYGN DALMPSLTET KTTVELLPVN GEFSLDDLQP WHSFGADSVP ANTENEVEPV DARPAADRGL TTRPGSGLTN Beta-Amyloid (1-42) IKTEEISEVK MDAEFRHDSG YEVHHQKLVF FAEDVGSNKG AIIGLMVGGV VIATVIVITL Beta-Amyloid, Prepro (727-770) VMLKKKQYTS IHHGVVEVDA AVTPEERHLS KMQQNGYENP TYKFFEQMQN Beta-Amyloid, Prepro (740-770)	480 510 540 570 600 630 660 690 720 750



AICD levels are increased in human AD brains. (A) Brain lysates from 13 AD patients (AD) and 12 non-dementia control subjects (Non-AD) were analyzed by SDS/PAGE and Western blotted with 0443 antibody (top rows) that recognizes APP-C terminus or AT-8 antibody (bottom rows). Blots were stripped and reprobed with GAPDH (middle rows). The upper rows show APP-CTF and AICD levels, which were quantified by NIH ImageJ software (B). Although there was a large variation in the AICD levels, they were significantly elevated in AD patients compared to non-demented controls (P = 0.0017). The lane marked with * in A (right panel) marks the non-AD sample with abnormally high AICD levels (an outlier). The wide variation in AD samples is also seen in phosphotau levels. (C) Summary of pathological events observed in FeCgamma25 mice. AICD expression is driven by a CaMKIIalpha promoter, which becomes active around P15, and activation of GSK-3Beta is observed at 6–8 weeks. Increased phosphorylation of tau is first observed at 3-4 months of age, although tau does not become aggregated until 7-8 months of age. Memory deficits become first apparent at this time point. Neuronal loss and up-regulation of NPY are not observed up to 12-15 months of age but become apparent >18 months of age. AD-related pathological features described in this study are shown in open ovals. Ghosal K., et al. PNAS, 2009,106 (43):18367-18372



Schematic diagram of APP sequential processing (not drawn in scale). EC: extracellular; TM: transmembrane; IC: intracellular. ABeta domain is highlighted in red. For simplicity, only one cleavage site is shown for each enzyme.

Hui Zheng and Edward H Koo, Mol Neurodegener. 2006; 1 : 5.

Catalog Number	Name	Standard Size
018-01	Amyloid beta-Protein (1-40) (Human)	200 µg
018-02	Amyloid beta-Protein (1-28) / Alzheimer⊡s Disease beta-Protein / SP-28 (Human)	200 µg
018-03	Amyloid beta-Protein [GIn11] (1-28) / Alzheimer S Disease beta-Protein / SP-28 (Human)	200 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
018-06	Amyloid beta-Protein (1-43) (Human)	200 µg
018-07	Amyloid beta-Protein (1-42) (Human)	200 µg
018-08	Amyloid beta-Protein (10-20) (Human)	500 µg
018-09	Amyloid beta-Protein / A4-Protein Precursor (328-332)	1 mg
018-65	Beta-Amyloid Precursor (430-467) (Human)	100 µg
018-66	Beta-Amyloid Precursor (471-494) (Human)	100 µg
018-67	Beta-Amyloid Precursor (497-520) (Human)	100 µg
018-68	Beta-Amyloid Precursor (740-770) / C-31 (Human)	100 µg
018-69	APP Intracellular Domain (AICD Short Form) / Beta-Amyloid Precursor (727-770) (Human)	100 µg
018-70	APP Intracellular Domain (AICD Long Form) / Beta-Amyloid Precursor (712-770) (Human)	100 ug
B-018-65	Beta-Amyloid Precursor (430-467) (Human) - Biotin Labeled	20 µg
B-018-66	Beta-Amyloid Precursor (471-494) (Human) - Biotin Labeled	20 µg
B-018-67	Beta-Amyloid Precursor (497-520) (Human) - Biotin Labeled	20 µg
B-018-68	Beta-Amyloid Precursor (740-770) / C-31 (Human) - Biotin Labeled	20 µg
B-018-69	APP Intracellular Domain (AICD Short Form) / Beta-Amyloid Precursor (727-770) (Human) - Biotin Labeled	20 µg
B-018-70	APP Intracellular Domain (AICD Long Form) / Beta-Amyloid Precursor (712-770) (Human) - Biotin Labeled	20 µg
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
G-018-01	Amyloid beta-Protein (1-40) (Human) - Purified IgG Antibody	400 µg
H-018-01	Amyloid beta-Protein (1-40) (Human) - Antibody for Immunohistochemistry	50 µl
T-018-01	Amyloid beta-Protein (1-40) (Human) - I-125 Labeled	10 µCi
T-018-07	Amyloid beta-Protein (1-42) (Human) - I-125 Labeled	10 µCi
T-018-65	Beta-Amyloid Precursor (430-467) (Human) - I-125 Labeled	10 µCi
T-018-66	Beta-Amyloid Precursor (471-494) (Human) - I-125 Labeled	10 µCi
T-018-67	Beta-Amyloid Precursor (497-520) (Human) - I-125 Labeled	10 µCi
T-018-68	Beta-Amyloid Precursor (740-770) / C-31 (Human) - I-125 Labeled	10 µCi
T-018-69	APP Intracellular Domain (AICD Short Form) / Beta-Amyloid Precursor (727-770) (Human) - I-125 Labeled	10 µCi
T-018-70	APP Intracellular Domain (AICD Long Form) / Beta-Amyloid Precursor (712-770) (Human) - I-125 Labeled	10 µCi
T-G-018-01	Amyloid beta-Protein (1-40) (Human) - I-125 Labeled Purified IgG	10 µCi