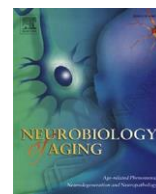


Contents lists available at [ScienceDirect](#)

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging

SET translocation is associated with increase in caspase cleaved amyloid precursor protein in CA1 of Alzheimer and Down syndrome patients

Patricia Facchinetti^a, Emilie Dorard^a, Vincent Contremoulins^b, Marie-Claude Gaillard^c, Nicole Déglon^c, Véronique Sazdovitch^d, Chantal Guihenneuc-Jouyaux^e, Emmanuel Brouillet^c, Charles Duyckaerts^d, Bernadette Allinquant^{a,*}

^aINSERM UMR 894, Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine, Paris, France

^bImagoSeine, Institut Jacques Monod, UMR 7592, CNRS and Université Paris Diderot, Paris, France

^cURA CEA CNRS 2210, Fontenay-aux-Roses, France

^dLaboratoire de Neuropathologie Escourolle, Hôpital de la Salpêtrière, AP-HP, and Centre de Recherche de l'ICM (UPMC, INSERM UMR S 975, CNRS UMR 7225), Paris, France

^eEA 4064, Université Paris Descartes, Sorbonne Paris Cité, Faculté des Sciences Pharmaceutiques et Biologiques, Paris, France

Article info

Article history:

Received 29 May 2013

Received in revised form 26 August 2013

Accepted 31 August 2013

Keywords:

SET translocation

Caspase cleaved APP

Alzheimer disease

Down syndrome

Hippocampus

Tau hyperphosphorylation

Abstract

Caspase cleaved amyloid precursor protein (APP_{cc}) and SET are increased and mislocalized in the neuronal cytoplasm in Alzheimer Disease (AD) brains. Translocated SET to the cytoplasm can induce tau hyperphosphorylation. To elucidate the putative relationships between mislocalized APP_{cc} and SET, we studied their level and distribution in the hippocampus of 5 controls, 3 Down syndrome and 10 Alzheimer patients. In Down syndrome and Alzheimer patients, APP_{cc} and SET levels were increased in CA1 and the frequency of both localizations in the neuronal cytoplasm was high in CA1, and low in CA4. As the increase of APP_{cc} is already present at early stages of AD, we overexpressed APP_{cc} in CA1 and the dentate gyrus neurons of adult mice with a lentiviral construct. APP_{cc} overexpression in CA1 and not in the dentate gyrus induced endogenous SET translocation and tau hyperphosphorylation. These data suggest that increase in APP_{cc} in CA1 neurons could be an early event leading to the translocation of SET and the progression of AD through tau hyperphosphorylation.

© 2013 Elsevier Inc. All rights reserved.

[Lien vers l'article](#)