Ved Chauhan et al., J Alzheimers Dis Parkinsonism 2018, Volume 8
DOI: 10.4172/2161-0460-C8-057

Potential therapeutic implications of gelsolin in Alzheimer's disease

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Deposition of fibrils Amyloid Beta-protein (Aβ) as amyloid plaques in the brain is a prominent feature in the pathology of AD. Gelsolin a multifunctional actin-binding protein is present as circulatory protein in plasma (p-gelsolin) and its shorter form is present in the cytoplasm (c-gelsolin). We have reported that gelsolin forms a complex with Aβ and gelsolin inhibits A fibrillization and it also solubilizes preformed Aβ fibrils. These findings suggest anti-amyloidogenic property of gelsolin. Other studies have also shown reduced amyloid load with peripheral administration of p-gelsolin or transgene expression of c-gelsolin in the transgenic mouse model of AD. The levels of gelsolin can also be increased epigenetically by inhibition of histone deacetylases, such as Trichostatin A (TSA). TSA has been reported to increase gelsolin expression in cell cultures and brain. We studied whether TSA can act as a potential therapeutic agent in AD through clearance of Aβ by affecting the levels of plasma/brain gelsolin in APPswe/PS1δE9 transgenic mouse model of AD. Intraperitoneal administration of TSA to these AD-tg mice for two months improved the learning ability during the Morris water maze training process. The western blots showed increased plasma levels of gelsolin, Aβ 1-40/Aβ 1-42 in TSA-treated mice as compared with vehicle-treated control mice. A positive correlation was observed between the plasma levels of gelsolin and Aβ 1-40 / Aβ 1-42 in AD-tg mice. These results suggest that TSA may help in Aβ clearance by inducing the expression of gelsolin, thus improving the learning skills. It seems that plasma gelsolin probably acts as peripheral sink protein to bind Aβ peptides and therefore help in Aβ clearance.

Biography

Ved Chauhan is the head of the Cellular Neurochemistry Laboratory at New York State Institute for Basic Research in Developmental Disabilities, New York. He has received his PhD from Post Graduate Institute of Medical Education and Research, India. After working as a Research Associate for two years at the University of Southern California, he joined IBR as a Research Scientist. He has published over 100 research articles in the field of signal transduction, membrane biochemistry, Alzheimer's disease and autism. For his work on Alzheimer's disease and Autism, he has been awarded several research grants as Principal Investigator from NIH, Alzheimer's Association and Autism Research Institute. He has also served as an Editorial Board Member of many journals.

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