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Potential therapeutic implications of gelsolin in Alzheimer's Disease

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Amyloid beta-protein (Aβ) gets fibrillized and deposited in the brains of individuals with Alzheimer's disease (AD) and in adult Down syndrome (DS) patients. Gelsolin, a multifunctional actin-binding protein, is present as a circulatory protein in plasma (p-gelsolin) and its shorter form is present in the cytoplasm (c-gelsolin). We have previously reported that (a) gelsolin forms a complex with Aβ, and (b) gelsolin can inhibit Aβ fibrillization, which suggests its anti-amyloidogenic property. 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. Gelsolin also exhibits neuroprotective effect under oxygen-glucose deprivation. During apoptosis, c-gelsolin is proteolytically cleaved into N (amino)- and C (carboxyl)-terminal fragments by activated caspase-3 or calpain. Our studies have demonstrated that gelsolin gets proteolytically cleaved in the brains of subjects with AD and DS. Oxidative stress and apoptosis are known to be involved in the pathogenesis of AD. We have also reported that gelsolin expression is increased under oxidative stress and apoptotic conditions in various cells. Further studies to understand H_2O_2-induced gelsolin expression suggest involvement of protein kinase C but not of MAP kinases in this process. In this presentation, the anti-amyloidogenic, anti-oxidative and anti-apoptotic role of gelsolin in AD will be discussed.

Biography

Dr. Ved Chauhan is the Head of the Cellular Neurochemistry Laboratory at the New York State Institute for Basic Research in Developmental Disabilities, Staten Island, NY. He received his Ph.D. in 1980 from Post Graduate Institute of Medical Education and Research, Chandigarh, India. Dr. Chauhan has published over 90 research articles in the field of signal transduction, membrane biochemistry, Alzheimer's disease and autism. He is also the Co-editor of a book entitled, "Autism: Oxidative stress, inflammation and immune abnormalities". For his work on Alzheimer's disease, he has been awarded research grants as Principal Investigator from NIH and Alzheimer's Association.

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