Abstract

Conventional approaches to target Alzheimer's Disease rely on drugs which are either small molecules inhibiting specific enzymes or antibodies that disrupt aggregation cascade. However, such molecules suffer from poor targeting, non-specific drug effect(s), poor bioavailability. Another major issue is their poor serum stability and higher immunogenicity. Hence, there is a need for a novel class of molecules which makes use of a cell's own ability to degrade the target. Here we present a proof of concept study with a multifunctional peptide molecule that directs intracellular tau protein to ubiquitin-proteasomal degradation pathway, one of the major protein quality control mechanism of the cell. This leads to tau protein degradation by the proteasomal complex. The multi-functional peptide makes use of a novel cell penetrating peptide which is of human origin, E3 binding sequence, linker peptide and a short peptide sequence with affinity towards β-tubulin region of tau protein. Moreover, this study also details studies related to the in-house establishment of a neuronal cell culture model based on SH-SY5Y, a human neuroblastoma cell line.

Keywords: Alzheimer's, Tau protein, Cell Penetrating Peptide, multifunctional peptide, proteasome, neuroblastoma cell line