Alzheimer’s disease is characterized by deposition of the b-amyloid peptide that derives from the amyloid precursor protein (APP) into plaques, and is genetically linked to the gene for apolipoprotein E (apoE). We have identified a novel apolipoprotein E-binding protein (NTRP) that also forms a complex with APP. NTRP was found to co-migrate with APP during native gel electrophoresis of rat brain extracts, and co-immunoprecipitated with APP from transfected human cell lysates. NTRP bound apoE in an isoform-specific manner \textit{in vitro} and co-immunoprecipitated with apoE from cell lysates. Co-expression of apoE and NTRP stimulated b-amyloid production from the 99-amino acid C-terminal fragment of APP that is the direct precursor to b-amyloid by 1.5- to 2-fold (P< 0.001), this effect was greater with apoE4 than apoE3 (P=0.02), and more significant for Ab1-42 than Ab1-40. The interaction between NTRP and apoE may therefore contribute to b-amyloid production in Alzheimer’s disease.

The interaction between APP and NTRP is evolutionarily conserved. Mutation of, or RNAi targeted to, the Drosophila orthologue of NTRP, which we call dementin, have altered metabolism of the Drosophila orthologue of APP, the APP-like protein, and demonstrate severe lethal neurodevelopmental defects.