The histopathological hallmarks of Alzheimer’s disease (AD) are plaques and tangles made from β-amyloid (Aβ) peptides and the axonal microtubule (MT) associated protein, tau, respectively. Although the significance of plaques and tangles for AD symptoms is controversial, normal tau negatively regulates kinesin MT motors, and thus governs axonal membrane trafficking. It follows that tau malfunctioning in AD alters axonal transport, but how might that contribute to pathogenesis? To address this question, we investigated tau effects on lipid rafts, which are major sites of Aβ production, and are enriched for the signature AD proteins, APP, β-secretase, γ-secretase, ApoE, ApoER2, and the tyrosine kinase, fyn. Using cultured fibroblasts, and WT and tau KO neurons we found that tau expression and extracellular Aβ profoundly affect the molecular composition and intracellular trafficking of lipid rafts. Raft levels of fyn, APP and ApoER2 were dramatically increased by tau expression, which also caused decreases in raft caveolin-1 and cholesterol, but had no effect on raft flotillin. Tau-CFP transfection of fibroblasts, which do not naturally express tau, caused a precipitous decrease in MT-dependent transport of caveolin-1-mDsRed and fyn-GFP. Treatment of WT neurons with Aβ42 dimer/trimers caused striking changes in raft fyn (increased) and APP (decreased), and a modest loss of raft flotillin. Tau thus somehow controls membrane domains where Aβ is produced and ApoE docks to cells. These results raise the intriguing possibilities that tau is directly linked to the pathway of Aβ production and controls ApoE functions by mechanisms that are sensitive to extracellular Aβ.