Sorting of the Alzhermer´s Disease Amyloid Precursor Protein Mediated by the AP-4 Complex.

A new Signal-Adaptor Interaction between Alzheimer's Disease Amyloid Precursor Protein and the AP-4 Complex has been published in the March edition of Developmental Cell, with Adriana L Rojas, manager of the macromolecular crystallography platform of CIC bioGUNE, as first co-author.

The paper reports the discovery of an entirely novel interaction between a signal from the cytosolic tail of the amyloid precursor protein (APP) and the μ4 subunit of the adaptor protein-4 (AP-4) complex. The novelty of this interaction lies not only in the properties of the APP signal but also in the nature of the binding site on μ4. Biochemical and X-ray crystallographic analysis reveals that the APP signal sequence and the location of the binding site on μ4 are distinct from those of other signal-adaptor interactions. In addition, disruption of this interaction leads to a shift in the distribution of APP from endosomes to the *trans*-Golgi network (TGN), and results in enhanced γ-secretase-catalyzed cleavage of APP to the pathogenic amyloid -β (Aβ) peptide. AP-4 thus emerges as a novel regulator of APP trafficking and reveals a whole new mode of signal recognition by adaptor proteins.

http://www.cell.com/developmental-cell/abstract/S1534-5807(10)00096-1

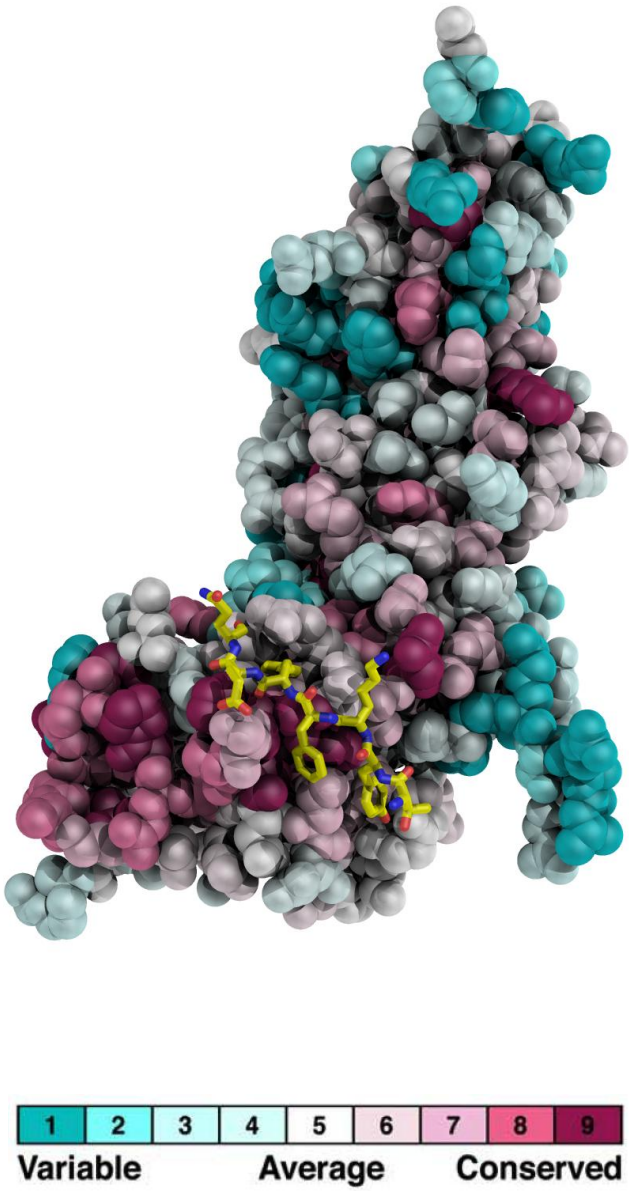

Fig1. Interaction of APP peptide with the μ4 C-terminal domain of AP4. Atoms of μ4 C-terminal domain are shown as spheres model, and colored according to the conservation scores. The bar shows the coloring scheme. The peptide from the cytosolic tail of APP (TYKFFEQ) is shown in stick representation (carbon, yellow; oxygen, red; nitrogen, blue)