The intracellular signaling mediated by FE65 - the function of FE65 in nuclei -

Tadashi Nakaya
(Lab. Neuroscience, Grad. Sch. Pharm. Sci, Hokkaido univ.)

FE65 is a neural adaptor protein and has three protein interaction domains, one WW domain at its middle region and two phosphotyrosine interaction domains at its carboxyl terminal region. It is shown that various types of proteins, such as membrane receptors, a kinase and a transcription factor interact with FE65 at these domains. The homologues of FE65 are conserved among many species, thus it was thought that FE65 had important roles *in vivo*. Unfortunately, FE65 deficient mice did not show any obvious phenotypes. Thus the physiological functions of FE65 are still unknown.

Amyloid precursor protein (APP) is one of FE65 interacting proteins and known as the precursor of Amyloid-β peptide, which is a causative factor for Alzheimer's disease. We and others reported that FE65 regulates the processing of APP and phosphorylation at Thr668 of APP cytoplasmic domain regulates the interaction between APP and FE65 (Ando *et al, J. Biol. Chem.*, 2001). Recently we reported that an osmotic stress induced the phosphorylation of APP and dissociation of FE65 from APP in cultured cells (Nakaya and Suzuki, *Genes Cells*, 2006). In this study, we will present the nuclear translocation of FE65 under an osmotic stress. Now we are going to reveal the molecular mechanisms of these intracellular signaling pathway.