Neurodegenerative Disease and ER stress

！ Shinsuke Matsuzaki, Taiichi Katayama, Futoshi Yukioka, Yoshihisa Koyama and Masaya Tohyama
(Anatomy and Neuroscience, Graduate School of Medicine, Osaka University.)

We have reported that mutations in Presenilin-1 (PS1) may increase vulnerability to ER stress by altering the UPR signalling pathway and accelerate the apoptosis via ER stress. We confirmed that human caspase-4, the most homologous gene to mouse caspase-12, is localized to the ER membrane and that is cleaved when cells are treated with ER stress-inducing reagents, but not with other apoptotic reagents and that caspase-4 can function as an ER stress-specific caspase in humans, and may be involved in pathogenesis of Alzheimer's disease. First, we show our results of investigations into the effects of PS1 mutation, Exon9 deleted PS1 (PS1 □E9), on the cleavage of caspase-4, activation of caspase-4, and the effects of caspase-4 on the caspase-9 and caspase-3. Next we present the involvement of ER stress in the pathogenesis of amyotrophic lateral sclerosis (ALS) and aggregation of SOD1 mutation (L84V). Last we show the functional involvement of ER stress to age-related macular degeneration (AMD).