

MOLECULAR SIGNALING OF CERAMIDE-INDUCED AUTOPHAGY: ROLE OF GSK3 β

Wei-Li Chen^{1,2} and *Chwen-Ming Shih*²

1) Graduate Institute of Medical Sciences, College of Medicine, Taipei Medical University, Taipei 110, Taiwan. 2) Department of Biochemistry, College of Medicine, Taipei Medical University

Cell death was subdivided into necrosis, apoptosis, and autophagy which has been demonstrated to play a pivotal role during the progress of neurodegenerative disease, such as Alzheimer's disease. The accumulation of autophagic vacuoles has been reported in typical neurodegenerative disease, but the mechanism remains unclear. In this study, cerebral endothelial cells (CECs) was employed as a cell model and was treated with ceramide to investigate the mechanism of ceramide-induced cell death. The cytotoxicity of ceramide induced autophagy and apoptosis in CECs as determined by flow cytometry, formation of autophagosomes and processing of LC3. Pharmacological inhibition of autophagy resulted in decrease of cell viability, suggesting autophagy serves as a cell protection in ceramide-treated CECs. The most important is that ceramide induced a decrease of the phosphorylated level at Ser9 of glycogen synthase kinase-3 β (GSK-3 β) which implied that GSK-3 β was activated during ceramide-induced autophagy. Besides, GSK-3 β inhibitors and siRNA were able to reduce the percentage of autophagy. These findings demonstrated that ceramide induced autophagy through activation of GSK-3 β in CECs which might be one of the crucial causes in cerebral angiopathy.

Keyword:

Ceramide, Cerebral endothelial cells, Autophagy, Glycogen synthase kinase-3 β .