Diallyl Trisulfide enhances Autophagy through AMPK Activation and Prevents Apoptosis in H9c2 Exposed to High Glucose

WW Kuo 1,* CY Huang2#, YH Tseng 1#

[1]Department of Biological Science and Technology, China Medical University,
[2] Graduate Institute of Basic Medical Science, China Medical University

Autophagy is a process of bulk degradation of intracellular components and shows protective effects in many organs under high glucose condition. Our previous *in vivo* and *in vitro* studies demonstrated that diallyl trisulfide (DATS) can attenuate high-glucose (HG)-induced cardiac apoptosis. However, whether autohpagy plays a protective role and is involved in the anti-apoptotic effect of DATS on HG-induced cell death is unknown. Using H9c2 cells, our data demonstrated that autophagy biomarker Atg1, Beclin-1, Atg5, LC3-II detected by western blot were increased after 33mM glucose treatment. The transfected GFP-LC3 detected by immunofluresence assay showed the similar result, indicating high glucose can induce autophagy. To determine the role of autophagy in the apoptosis development, we used 3-methyladenine (3-MA) as autophagy inhibitor and rapamycin as autophagy enhancer. The results of caspase 3 levels and TUNEL assay showed that cell death was enhanced by 3-MA and cell survival was promoted by rapamycin, indicating autophagy plays a protective role and improves apoptosis development in cells exposed to HG. Furthermore, increased level of LC-3-II by HG was further enhanced by DATS in a dose-dependently manner. It was also observed that abolished phosphorylation of Akt and AMPK, and increased caspase 3 by HG were reversed by DATS. Interestingly, the treatment of small interference RNA of AMPK abolished the LC3-II formation and protective effect of DATS on HG-induced cell death. Taken together, autophagy mediated by AMPK is involved in the protective effect of DATS on H9c2 cells exposed to HG.