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PERK MEDIATED ENDOPLASMIC RETICULUM STRESS IS INVOLVED IN ANGIOTENSIN II INDUCED CARDIAC HYPERTROPHY

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Objectives To investigate the role of protein kinase R-like ER kinase (PERK)-mediated endoplasmic reticulum stress (ERS) in angiotensin II, and to explore the role of taurine (Tau), the ERS inhibitor, in Ang II-induced cardiomyocyte hypertrophy.

Methods In the model of Ang II-induced cardiomyocyte hypertrophy from neonatal Sprague-Dawley rats, morphological studies, ³H-Leucine incorporation and surface area were employed to assess cardiac hypertrophy. Real time PCR, RT-PCR and Western blotting were used to detect mRNA and protein expression of glucose-regulated protein 78 (GRP78), calreticulin (CRT), PERK, eukaryotic initiation factor 2 α (eIF2 α), (C/EBP) homologous protein (CHOP). Cultured cardiomyocytes were treated with Tau prior to Ang II treatment, and then detected the status of cardiomyocytes and ER stress-related molecular.

Results Compared with control group, angiotensin II treated cardiomyocytes showed that CRT mRNA and protein expression increased by 146.4% and 125.3%, respectively ($p < 0.05$); GRP78 mRNA and protein expression increased by 84% and 77.6%, respectively ($p < 0.05$). And PERK mRNA and protein expression increased by 165.4% and 132.1%, respectively ($p < 0.05$); eIF2 α mRNA and protein expression were increased by 110.9% and 46.5%, respectively ($p < 0.05$); CHOP mRNA and protein expression increased by 117.7% and 63.3%, respectively ($p < 0.05$). Compared with Ang II group, Ang II+Tau group showed that ANP and BNP mRNA expression decreased by 57.5% and 38.4%, respectively ($p < 0.05$), protein synthesis rate decreased by 32.5% ($p < 0.05$), surface area decrease by 33% ($p < 0.05$). And taurine decreased mRNA and protein expression levels of CRT in Ang II-induced cardiomyocytes by 57.6% and 43.1% ($p < 0.05$), those of GRP78 by 60.6% and 33.3% ($p < 0.05$), those of PERK by 31.7% and 43.5% ($p < 0.05$), those of eIF2 α by 56.2% and 17.8% ($p < 0.05$), those of CHOP by 62.7% and 37.4% ($p < 0.05$).

Conclusions Ang II treatment up-regulated the mRNA and protein level of CRT, GRP78, PERK, eIF2 α and CHOP in cardiomyocytes, indicating that Ang II could induce ER stress response in cultured cardiomyocytes. Tau down-regulated expression of ANP and BNP, protein synthesis rate, and cell surface area induced by Ang II. Tau also down-regulated expression of ER stress-related molecules. Our data indicated that PERK-mediated ERS is involved in Ang II-induced cardiomyocyte hypertrophy, and Tau attenuated Ang II-induced cardiomyocyte hypertrophy through suppressing ERS.