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## Distinct roles of canonical and non-canonical macroautophagy induced by angiotensin II in H9c2 cardiomyoblast cells

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Macroautophagy (hereafter referred to as autophagy) has emerged as an important process in the pathogenesis of cardiovascular diseases, but the detailed pathomechanisms are not fully understood. Angiotensin II has been well known its importance on the pathogenesis of heart disease by promoting cardiomyocyte hypertrophy, fibrosis, apoptosis. To further investigate whether autophagy is involved in AngII-induced myocardial cell death, pharmacological autophagy inhibitor (3-methyladenine, 3MA) and inducer (Rapamycin, Rapa) as well as ATGs (Autophagy related genes) siRNA silencing canonical or non-canonical autophagy were applied in this study. We found that the both canonical autophagy markers (ATG5, LC3II) and non-canonical autophagy associated proteins (Rab9, LAMP2) were increased in a time dependent manner in AngII- treated H9c2 cells. In addition, Trypan Blue Exclusion assays revealed that prompting canonical autophagy by Rapa restores cell viability significantly while 3-MA shown minor effects on the cell viability of AngII-treated H9c2 cells. Meanwhile, TUNLE assay as well as Western blot assay indicated that Rab9 or Beclin-I siRNA silencing reduced apoptosis level markedly in AngII-treated H9c2 cells. On the contrast, ATG5 silencing increased AngII–induced apoptosis level in H9c2 cells. Taken together, these results suggested that AngII-induced non-canonical autophagy is deleterious to myocardial cells and canonical autophagy may be the compensated protection in response to AngII challenge. This study provides the first evidence that the possible distinct roles of stress-induced canonical and non-canonical autophagy in myocardial cells and its may help the development of future therapeutic autophagy agonists/antagonists to cure cardiomyopathy.