題名:Angiotensin II activates myostatin expression in cultured rat neonatal cardiomyocytes via p38 MAP kinase and myocyte enhance factor 2 pathway

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摘要:Angiotensin II (AngII) plays a critical role in cardiac remodeling and promotes cardiac myocyte hypertrophy. Myostatin, a negative regulator of muscle growth, is increased in hypertrophied and infarcted heart. The direct effect of AngII on cardiac myocyte myostatin expression has not been previously investigated. We hypothesized that myostatin may act as a cardiac endocrine inhibitor for AngII. AngII-induced myostatin protein expression in cultured rat neonatal cardiomyocytes was dose-dependent. AngII significantly increased myostatin protein and mRNA expression in a time-dependent manner. Addition of losartan, SB203580, or p38 siRNA 30 min before AngII stimulation significantly blocked the increase of myostatin protein by AngII. AngII significantly increased phosphorylation of p38 while SB205380 and losartan attenuated the phosphorylation of p38 induced by AngII. AngII increased, while myostatin-Mut plasmid, SB203580, losartan, and myocyte enhance factor 2 (MEF-2) antibody abolished the myostatin promoter activity. Co-stimulation with myostatin and AngII significantly inhibited the protein synthesis induced by AngII. In conclusion, AngII enhances myostatin expression in cultured rat neonatal cardiomyocytes. The AngII-induced myostatin is mediated through p38 MAP kinase and MEF-2 pathway.