Mechanical stretch enhances the expression of resistin gene in cultured cardiomyocytes via tumor necrosis factor-alpha

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摘要

Abstract

The heart is a resistin target tissue and can function as an autocrine organ. We sought to investigate whether cyclic mechanical stretch could induce resistin expression in cardiomyocytes and to test whether there is a link between the stretch-induced TNF- and resistin. Neonatal Wistar rat cardiomyocytes grown on a flexible membrane base were stretched by vacuum to 20% of maximum elongation at 60 cycles/min. Cyclic stretch significantly increased resistin protein and mRNA expression after 2–18 h of stretch. Addition of PD-98059, TNF- antibody, TNF-receptor antibody, and ERK MAP kinase small interfering RNA 30 min before stretch inhibited the induction of resistin protein. Cyclic stretch increased, whereas PD-98059 abolished, the phosphorylated ERK protein. Gel-shift assay showed a significant increase in DNA-protein binding activity of NF-B after stretch, and PD-98059 abolished the DNA-protein binding activity induced by cyclic stretch. DNA binding complexes induced by cyclic stretch could be supershifted by p65 monoclonal antibody. Cyclic stretch increased resistin promoter activity, whereas PD-98059 and p65 antibody decreased resistin promoter activity. Cyclic stretch significantly increased TNF- secretion from myocytes. Recombinant resistin protein and conditioned medium from stretched cardiomyocytes reduced glucose uptake in cardiomyocytes, and recombinant small interfering RNA of resistin or TNF- antibody reversed glucose uptake. In conclusion, cyclic mechanical stretch enhances resistin expression in cultured rat neonatal cardiomyocytes. The stretch-induced resistin is mediated by TNF-, at least in part, through ERK MAP kinase and NF-B pathways. Glucose uptake in cardiomyocytes was reduced by resistin upregulation.