Aims To determine the influence of high glucose and interleukin 1β (IL-1β) on human cardiac fibroblasts functions and the effects of eplerenone in these responses.

Methods and results Human cardiac fibroblasts were cultured in normal or high glucose media in the absence or presence of IL-1β and/or eplerenone. MMP-2 activities were determined by using in-gel zymography. mRNA expression of MMP-2 and TIMP-2 were evaluated by rt-PCR. Results show that high glucose stimulates the activity of MMP-2 and accelerates MMP-2 mRNA synthesis. When Equimolar mannitol was used as an osmotic control, the activity enhancement of MMP-2 were also observed. We have also found that MMP-2 activity and mRNA expression were improved significantly (~2×) by using the combination of high glucose and IL-1β as compared with using high glucose or IL-1β alone. Increase of MMP-2 activity and mRNA expression were blocked by eplerenone, that is, neither high glucose nor IL-1β has impacted TIMP-2 mRNA expression in the experiments.

Conclusions High glucose increases the activity of MMP-2 by means of regulating MMP-2 mRNA expression in human cardiac fibroblasts through osmotic and non-osmotic pathways. Combining IL-1β with high glucose was found to increase significantly the MMP-2 activity and mRNA expression in human cardiac fibroblasts as compared with using IL-1β or high glucose in dividedly. However, such induced effects can be readily normalised by the use of Eplerenone.

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THE ROLE OF EPLERENONE ON ACTIVITY OF MATRIX METALLOPROTAINASE-2 STIMULATED BY HIGH GLUCOSE AND INTERLEUKIN 1β IN HUMAN CARDIAC FIBROBLASTS

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