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HUMAN TISSUE KALLIKREIN 1 GENE OVEREXPRESSION IMPROVES VENTRICULAR REMODELLING WITH MYOCARDIAL INFARCTION IN RATS

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Objectives Tissue kallikrein 1 cleaves kininogen substrate to produce vasoactive kinin peptides that have been implicated in protecting against ischaemia/reperfusion-induced cardiomyocyte injury. The objective of this study was to explore the effect of recombinant

adenovirus-mediated human tissue kallikrein-1 (Ad-hTK1) on ventricular remodelling in rats after myocardial infarction (MI).

Methods Rats were subjected to ligating left anterior descending artery of coronary artery. 1×10^{10} PFU Ad-hTK1 or control virus (Ad-EGFP) were injected at multiple sites into the infarcted myocardium 1 h after the operation. Four-weeks after the intervention, the protein expression of hTK1 was detected by Western-blotting analysis. A serial frozen sections, histological morphometric observation were carried out using fluorescence microscope and HE staining. Collagen were detected by Sirius red-statured picric staining, and the number of myocardial microvessel was detected by CD34-FITC antibody immunocytochemistry assay.

Results The expression of green fluorescence and hTK1 protein were observed in MI-hTK1 rats. There were no differences in body weight among the groups at 4 weeks after MI. As compared with sham groups, MI resulted in increases in heart weight, LVW and LVWI, inflammation cells and collagen density, in decreases capillary density, at 4 weeks after MI. However, kallikrein gene delivery tended to reduce heart weight, LVW, LVWI, inflammation cells and collagen density at 4 weeks after MI. Capillary density in MI-hTK1 rats was also significantly increased than in the MI with control virus.

Conclusions This study indicates that recombinant adenovirus-mediated human tissue kallikrein-1 overexpression plays an important role in preventing the progression of MI by attenuating cardiac hypertrophy and fibrosis, improving neovascularisation.