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MICRORNA-26 REGULATES RAT CARDIAC REMODELLING BY SUPPRESSING GLYCOGEN SYNTHASE KINASE 3β

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Objectives MicroRNA-26 (miR-26) was found to be down-regulated in the myocardium in cardiac remodelling animal models. Here we investigated the critical role of miR-26a/b on cardiac remodelling in vivo and in vitro.

Methods Rats which underwent sham or transverse abdominal aortic constriction (TAAC) surgery were divided into control and TAAC group. Cardiomyocytes (CMs) and cardiac fibroblasts (CFs) were isolated from neonatal Sprague-Dawley rats. QPCR assay was applied to detect the expression levels of miR-26 a/b in the myocardial tissue and plasma of TAAC rats, and in CMs and CFs treated with angiotesinII(AngII). Gain- and loss-of-function studies were applied through overexpressing or inhibiting miR26a/b or Glycogen Synthase Kinase 3β (GSK3β) by liposomes transfecting.

Results The data demonstrated that the expressive levels of miR-26a/b were down-regulated in cardiac tissues and plasma in TAAC rats, moreover in CMs and CFs treated with AngII. Furthermore, overexpression miR26a/b by transfected miR-26a/b mimics in CM or CF inhibited CM hypertrophy or CF collagen synthesis significantly, and down-regulating the expressive levels of miR-26a/b by transfected miR-26a/b inhibitors in CM or CF led to opposite effects, suggesting that miR-26 was an anti-hypertrophy and anti-fibrosis gene. Through luciferase assay our study suggested that Glycogen Synthase Kinase 3β (GSK3β) gene that was negatively regulated by miR-26 in CM and CF may be a direct target of miR-26. Overexpression of miR-26 attenuates the endogenous GSK3β mRNA and protein levels followed by the inhibition of CM hypertrophy and CF collagen synthesis. Down-regulation of miR-26 reversed these effects. Furthermore, silence of GSK3β gene phenocopied the anti-hypertrophy and anti-fibrosis effects of miR-26, whereas overexpression of this protein attenuated the effects of miR-26.

Conclusions Our data highlight an important role of miR-26 in the control of pathological structural changes in rat heart, which may associated with suppressing the GSK3β signalling pathway, and implicate the potential application of miR-26 in diagnosis and therapy of cardiac remodelling.