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INHIBITORS OF MIRNA-30 FAMILY PROTECTED THE HYPOXIA-INDUCED INJURY ON CARDIAC MYOCYTES VIA INCREASING THE EXPRESSION OF CSE

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Objectives Recently, miRNAs and H_2S have been reported to be cardioprotective during myocardial infarction injury. However, there is little evidence indicating a functional role for miRNA in regulating the generation of H_2S. Our study was designed to determine

which miRNAs are able to protect myocardial ischaemic injury by regulating the expression of CSE (Cystathionine gamma-lyase, a major H_2S-producing enzyme in the cardiovascular system).

Methods Using real time PCR, we found that the miR-30 family, which includes 5 closely related miRNAs were highly expressed in the non-infarct and border zone regions after 48 h of ischaemia injury. Computational prediction implied CSE as potential targets for miR-30 family, and luciferase activity assay identified that CSE was a direct target of miR-30 family. Overexpression of miR-30 family by transfecting miRNA mimics for 48h in cultured neonatal rat cardiomyocytes demonstrated an inhibition of the expression of CSE at both mRNA and protein levels, and also a reduction of the H_2S generation. In contrast, downregulation of miR-30 family by antisense inhibitors increased the level of CSE mRNA and protein and the H_2S concentration. MTT results show that hypoxia-induced cardiac cell death was increased by miR-30 family mimics and was decreased by miR-30 family inhibitors.

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Conclusions MiRNA-30 family regulated the generation of H_2S via its target gene CSE, their protective effect against the hypoxia-induced injury on cardiomyocytes may open a new therapeutic avenue for the treatment of myocardial infarction injury.