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 H2S 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 H2S. 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 H2S-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 48h 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 H2S generation. In contrast, downregulation of miR-30 family by antisense inhibitors increased the level of CSE mRNA and protein and the H2S 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.

**Results** 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 48h 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 H2S generation. In contrast, downregulation of miR-30 family by antisense inhibitors increased the level of CSE mRNA and protein and the H2S 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.

**Conclusions** MiRNA-30 family regulated the generation of H2S 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.