MicroRNA-25 Gene Therapy Improves Cardiac Function and Reduces Infarct Size in Mice

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MicroRNAs (miRs) are small non-coding RNAs that regulate a wide range of physiological and pathophysiological processes by post transcriptional gene silencing. microRNA 106b~25 cluster is among the most abundant microRNAs in endothelial cells but it's function is not fully understood.

In the current study we investigated the expression of miR 106b~25 in cardiac muscle following myocardial infarction by real time PCR. Additionally, we examined the effect of miR 106b~25 overexpression on the angiogenic capacity and resistance to h2o2 induced cell death in endothelial cells. The possible angiogenic effects were further tested by employing in-vivo Matrigel assay in miR 106b~25 knockout mice.

Finally, we investigated whether intramyocardial gene transfer of naked DNA encoding miR-25 could promote a functional recovery follwoing MI. We report the downregulation of miR 106b~25 cluster following MI. In addition, overexpression of miR 106b~25 cluster in endothelial cells improved their proliferation and migration towards VEGF. Overexpression also improved endothelial cell survival following h2o2 induced damage and reduced apoptosis levels in 293HEK cells. Finally, miR-25 gene transfer to the peri-infarct region after MI induction in mice resulted in improved ventricular function, evident by echocardiography and reduced infarct size as seen in masson trichrome staining.

In conclusion, miR 106b~25 enhances angiogensis, protects endothelial cells and improves cardiac function following MI. miR 106b~25 gene therapy may stand as a novel target for future gene based therapies in regenerative cardiology.