miR-133a overexpression impairs endothelial cell migration and tube formation in vitro

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Emerging evidence indicates that short (~22 nucleotides) non-coding RNA molecules called microRNAs (miRNAs) play a key role in the regulation of post-ischaemic angiogenesis. miRNAs control gene expression by binding to complementary sequences of specific mRNA transcripts, leading to degradation or translational repression of the targeted mRNA. miR-133a is highly expressed and plays a crucial role in skeletal and cardiac muscle biology. The expression level of miR-133a in vascular endothelial cells is very low under physiological conditions. However, multiple cardiovascular risk factors including oxidized-LDL, pro-inflammatory cytokines, hyperglycemia, dyslipidemia, and hyperhomocysteinemia induce aberrant miR-133a expression in endothelial cells leading to endothelial dysfunction. Endothelial dysfunction in cardiovascular ischaemic disease is often accompanied by impairment of reparative angiogenic processes.

Here, we have evaluated the role of aberrant miR133a expression in VEGF-mediated angiogenesis. We show that exogenous expression of miR-133a in Human Umbilical Vein Endothelial Cells (HUVEC) significantly reduces VEGF-induced endothelial cell proliferation. Moreover, adenoviral-mediated delivery of cardiac miR133a into endothelial cells inhibits HUVEC cell motility and tubular morphogenesis. Interestingly, downregulation of phosphorylation (activation) of the signalling protein Erk1/2 by miR-133a was detected in VEGF stimulated HUVEC cells.

Our results demonstrate that aberrant expression of miR133a has an anti-angiogenic effect in endothelial cells, and strongly suggest that targeted strategies to suppress ectopic expression of miR-133a in the dysfunctional endothelium might have important therapeutic applications to improve reparative angiogenic process in patients suffering from ischaemic cardiovascular disease.

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