Insight… miR-145 may be transferred from VSMCs to macrophages

LDL-receptor-deficient mice lacking microRNA-143/145 have less atherosclerosis

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MicroRNAs (miRNAs, miRs) have emerged as important post-transcriptional regulators of gene expression. In vascular pathologies, the miR-143/145 cluster has attracted particular attention. The miR-143/145 cluster is encoded by a bicistronic transcript, and regulates the differentiation, plasticity and contractile function of vascular smooth muscle cells (VSMCs). VSMCs from miR-143/145–deficient mice were locked in a synthetic state, which favoured neointimal lesion development despite normal levels of serum cholesterol and lipoproteins (1). In contrast, deficiency of miR-143/145 on the low-density lipoprotein receptor (*Ldlr*$^{-/-}$) background reduced VLDL and LDL cholesterol (2). When Sala et al. crossed *miR-143/145*$^{-/-}$ mice with Ldlr$^{-/-}$ mice, the double knock-out mice had less atherosclerosis. Bioinformatic prediction algorithms identified the ATP-binding cassette transporter ABCA1 as a potential target of miR-145. Functional and luciferase experiments confirmed a direct interaction of miR-145 with the 3'UTR of *ABCA1*. In tissues from *Ldlr*$^{-/-}$ mice, miR-145 levels were significantly higher in the aorta than in liver or macrophages. In the double knock-out mice, ABCA1 expression was markedly increased in the aorta and the liver, but there was no change in HDL cholesterol although *ABCA1* promotes cellular cholesterol efflux. The macrophage content in atherosclerotic plaques, however, was decreased. Based on an *in vitro* approach, the authors postulated that miR-145 may be transferred from VSMCs to macrophages. A similar transfer of miR-143/145 had previously been reported for endothelial cells: miR-143/145 secreted in exosomes of endothelial cells could apparently regulate VSMC function (3). It is currently unclear whether such a miRNA transfer between vascular cell types is just an *in vitro* phenomenon or also occurs *in vivo* to modify gene expression. In summary, therapeutic strategies targeting miR-145 to maintain a contractile VSMC phenotype have to be re-evaluated in the context of dyslipidaemia.

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Conflicts of interest

None declared.

References

1. Boettger T, Beetz N, Kostin S, et al. Acquisition of the contractile phenotype by murine arterial smooth muscle cells depends on the Mir143/145 gene cluster. J Clin Invest 2009; 119: 2634-2647.
2. Sala F, Aranda JF, Rotllan N, et al. MiR-143/145 deficiency protects against progression of atherosclerosis in Ldlr-/-mice. Thromb Haemost 2014; 112: 796-802.
3. Hergenreider E, Heydt S, Tréguer K, et al. Atheroprotective communication between endothelial cells and smooth muscle cells through miRNAs. Nat Cell Biol 2012; 14: 249-256.

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