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.

Conflicts of interest
None declared.

References