MicroRNAs regulating lipid metabolism in atherogenesis.


Source

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Abstract

MicroRNAs have emerged as important post-transcriptional regulators of lipid metabolism, and represent a new class of targets for therapeutic intervention. Recently, microRNA-33a and b (miR-33a/b) were discovered as key regulators of metabolic programs including cholesterol and fatty acid homeostasis. These intronic microRNAs are embedded in the sterol response element binding protein genes, SREBF2 and SREBF1, which code for transcription factors that coordinate cholesterol and fatty acid synthesis. By repressing a variety of genes involved in cholesterol export and fatty acid oxidation, including ABCA1, CROT, CPT1, HADHB and PRKAA1, miR-33a/b act in concert with their host genes to boost cellular sterol levels. Recent work in animal models has shown that inhibition of these small non-coding RNAs has potent effects on lipoprotein metabolism, including increasing plasma high-density lipoprotein (HDL) and reducing very low density lipoprotein (VLDL) triglycerides. Furthermore, other microRNAs are being discovered that also target the ABCA1 pathway, including miR-758, suggesting that miRNAs may work cooperatively to regulate this pathway. These exciting findings support the development of microRNA antagonists as potential therapeutics for the treatment of dyslipidaemia, atherosclerosis and related metabolic diseases.

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