

9. RP5-833A20.1/miR-382-5p/NFIA-dependent Signal Transduction Pathway Contributes to the Regulation of Cholesterol Homeostasis and Inflammatory Reaction.

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文章简介

本研究通过基因芯片筛选发现巨噬细胞源性泡沫细胞与巨噬细胞相比较，**lncRNA RP5-833A20.1** 表达上调而核因子 IA (NFIA) 表达下调；此外，一系列实验证实 **lncRNA RP5-833A20.1** 可通过体外诱导 **hsa-miR-382-5p** 表达来抑制 NFIA 表达，**RP5-833A20.1 / hsa-miR-382-5p / NFIA** 途径对于调节巨噬细胞胆固醇稳态和炎症反应至关重要。动物实验表明，过表达 NFIA 可以增加高密度脂蛋白胆固醇水平，降低低密度脂蛋白胆固醇和极低密度脂蛋白胆固醇水平，减少炎症性细胞因子的水平，增强反向胆固醇转运，并抑制小鼠动脉粥样硬化病变进展。提示 **RP5-833A20.1 / miR-382-5p / NFIA** 途径对于调节胆固醇稳态和炎症反应至关重要，可能是动脉粥样硬化等心血管疾病的治疗新靶点。

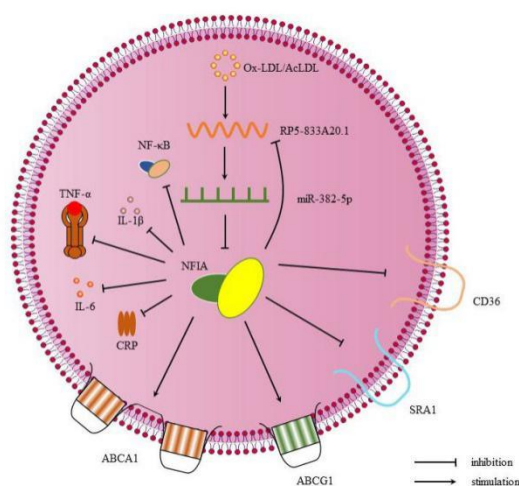


Fig. Schematic representation for regulation effects of RP5-833A20.1/miR-382-5p/NFIA on cholesterol homeostasis and inflammatory reactions. The results of the present study revealed the following scheme for the possible mechanism by which Ox-LDL regulates cholesterol homeostasis and inflammatory reactions. When THP-1 macrophages were treated with Ox-LDL, biologically relevant signaling was mediated mainly via the RP5-833A20.1/miR-382-5p/NFIA pathway. Then, NFIA expression was suppressed, which in turn decreased

the expression of ABCA1 and ABCG1 and increased the expression of SRA1 and CD36, and finally promoted cholesterol uptake and inhibited apoA1- and HDL-mediated cholesterol efflux. At the same time, reduction of NFIA expression resulted in an increase in NF- κ B expression, which in turn promoted releasing inflammatory cytokines.