Distinctive miRNA signature associated to inflammation in monocytes exposed to atherogenic low density lipoproteins: miR126

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Purpose: Small non-coding microRNAs (miRNAs), that post-transcriptionally regulate gene expression, have emerged as key regulators of molecular pathways that may critically control monocyte differentiation and function in hypercholesterolemia, a major risk factor for atherosclerotic plaque evolution. The present study was aimed to investigate the differential miRNA signature profile in cultured human monocyte exposed to atherogenic concentrations of low density lipoproteins (LDL).

Methods: Human monocytes from healthy donors were isolated and exposed to atherogenic concentrations (180 mg/dL) of LDL during 24 hours. miRNA pattern was determined using a Taqman array micro fluidic card. Gene and protein analysis of in silico selected targets was performed by RT-PCR and western-blot.

Results: We consistently identified 73 miRNAs in human monocytes. Ten miRNAs were differentially upregulated and 1 downregulated, with >1.5 fold difference, after exposition to atherogenic concentrations of LDL. Among the differential miRNA pattern, miR-126 showed the largest changes (>3 fold increase, p<0.05). In silico IPA core analysis revealed inflammation as the most representative process associated to the LDL-induced differential miRNA profile (p<0.0001). By combining MiRNA Target Filter prediction and minimum free energy (mfe) analysis using RNAhybrid, we identified the member of the tumor necrosis factor receptor superfamily TNFRSF10B, receptor for ligands involved in cell-apoptosis pathway, as the gene regulated by miR-126 with a highest score. Monocyte exposed to LDL did not show any significant change in TNFRSF10B mRNA expression. However, TNFRSF10B protein level in monocytes was >2 fold decreased (p<0.05) after 24 h exposure to LDL, indicating its post-transcriptional regulation. Conclusions: our data suggest that the increase of miR-126 expression in monocyte exposed to atherogenic LDL might identify a novel mechanism involving the monocyte-dependent inflammatory response in hypercholesterolemia and regulate TNFRSF10B protein levels in monocytes.