ABSTRACT

Sunar S. Study of the Role of the 5-Lipoxygenase-Regulated MiRNAs on Monocytes/Macrophages and Endothelial Cell Interactions. Istanbul University, Institute of Health Sciences, Faculty of Pharmacy, Department of Pharmacology. PhD Thesis. Istanbul. 2026.

5-Lipoxygenase (5-LO) is an important enzyme in inflammatory processes due to its role in leukotriene biosynthesis. In addition to this role, 5-LO has been shown to play a role in the regulation of microRNAs (miRNAs). This study aims to investigate the effect of 5-LO on miRNA expression in monocytes and monocyte-derived small extracellular vesicles (sEV), and its effect on the inflammatory response in endothelial cells mediated by monocyte-derived sEV. For this, expression of specific miRNAs in Mono Mac 6 (MM6) wild-type and 5-LO knockout cells and sEV were evaluated. Human umblical vein endothelial cells (HUVEC) were stimulated with MM6-derived sEV, and inflammatory cytokine and chemokine levels were evaluated. Our findings showed that 5-LO increased expression of miR-99b in MM6 cells and expression of miR-125a in sEV. Furthermore, we showed that sEV released from MM6 cells in the presence of 5-LO reduced IL-6, IL-8, and MCP-1 levels in HUVECs. In conclusion, our study demonstrated that 5-LO can alter the miRNA content of monocyte-derived sEV, and these sEV can modulate the inflammatory response in endothelial cells. In conclusion, our findings can contribute to a better understanding of EV-mediated miRNA communication in vascular inflammation and development of 5-LO-based therapies for diseases such as atherosclerosis.

Key Words: 5-Lipoxygenase, MicroRNA, Small Extracellular Vesicle, Monocyte/Macrophage, Endothelial Cell

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