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The emerging crosstalk between atherosclerosis-related microRNAs and Bermuda triangle of foam cells: Cholesterol influx, trafficking, and efflux

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ABSTRACT

In atherosclerosis, the gradual buildup of lipid particles into the sub-endothelium of damaged arteries leads to numerous lipid alterations. The absorption of these modified lipids by monocyte-derived macrophages in the arterial wall leads to cholesterol accumulation and increases the likelihood of foam cell formation and fatty streak, which is an early characteristic of atherosclerosis. Foam cell formation is related to an imbalance in cholesterol influx, trafficking, and efflux. The formation of foam cells is heavily regulated by various mechanisms, among them, the role of epigenetic factors like microRNA alteration in the formation of foam cells has been well studied. Recent studies have focused on the potential interplay between microRNAs and foam cell formation in the pathogenesis of atherosclerosis; nevertheless, there is significant space to progress in this attractive field. This review has focused to examine the underlying processes of foam cell formation and microRNA crosstalk to provide a deep insight into therapeutic implications in atherosclerosis.

1. Introduction

Atherosclerosis is characterized by an inflammatory response induced by the retention of apolipoprotein B-containing lipid particles in vulnerable sections of the arterial walls [1]. The trapped lipoproteins are exposed to a variety of alterations, making them a pro-inflammatory signal which activates the endothelial cells [2]. The subsequent immunological reaction is the recruitment of monocytes into the sub-endothelial region, where they mature into macrophages and engulf the high level of native and modified low-density lipoproteins (LDLs), transforming them into lipid-laden foam cells [3]. While LDLs removal by macrophages is considered to be advantageous at the start of this immune reaction, the continuous removal of modified-LDLs induces the apoptosis and necrosis of foam cells [4,5]. Foam cells have a low migration capacity and play a pivotal role in necrotic core creation and atherosclerosis progression [6]. The ensuing disruption of lipoprotein metabolism affects the phenotype of macrophages and compromises critical immune activities [4]. Besides, it is now clear that recruiting

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