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REVIEW

Therapeutic approaches to drug targets in atherosclerosis

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Abstract Non-communicable diseases such as cancer, atherosclerosis and diabetes are responsible for major social and health burden as millions of people are dying every year. Out of which, atherosclerosis is the leading cause of deaths worldwide. The lipid abnormality is one of the major modifiable risk factors for atherosclerosis. Both genetic and environmental components are associated with the development of atherosclerotic plaques. Immune and inflammatory mediators have a complex role in the initiation and progression of atherosclerosis. Understanding of all these processes will help to invent a range of new biomarkers and novel treatment modalities targeting various cellular events in acute and chronic inflammation that are accountable for atherosclerosis. Several biochemical pathways, receptors and enzymes are involved in the development of atherosclerosis that would be possible targets for improving strategies for disease diagnosis and management. Earlier anti-inflammatory or lipid-lowering treatments could be useful for alleviating morbidity and mortality of atherosclerotic cardiovascular diseases. However, novel drug targets like endoglin receptor, PPARα, squalene synthase, thyroid hormone analogues, scavenger receptor and thyroid hormone analogues are more powerful to control the process of atherosclerosis. Therefore, the review briefly focuses on different novel targets that act at the starting stage of the plaque form to the thrombus formation in the atherosclerosis.

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Contents

1. Introduction

Cancer, diabetes, obesity, myocardial infarction, hyperlipidemia, chronic respiratory diseases and cardiovascular disease (CVD) like atherosclerosis are the major non-communicable diseases (NCD). These NCD are the leading causes of death worldwide in not only high-income population but in the middle and low group (Margaret, 2010). Atherosclerosis is the chronic inflammatory disease which overall increases the morbidity and the mortality rate (John, 2000).The development of the level of atherosclerosis from an early fatty streak lesion to a highly hazardous rupture-prone plaque is because of the many cellular and molecular events at each level hence, it is the inflammatory event (Robert, 2005). These fatty streaks are one of the signs of atherosclerosis, which is first observed by Russell Holman and this fatty streak develops, thrombosis or hemorrhage (Brian et al., 2012).

A persistent increase in circulating low-density lipoprotein (LDL) levels in the body is one of the most important causes for the initiation and progression of atherosclerosis. In this respect, macrophages play a very important role by increasing accumulation of lipids in blood vessels, leading to inflammation and plaque formation. There are two different theories proposed to describe the events involved in atherogenesis. The first hypothesis is "response to injury," in which endothelial lining's injury initiates events of deposition of LDL in the intimal space, followed by recruitments and migration of monocyte-derived macrophages, which take up modified LDL and become foam cells (John, 2000; Ross, 1993; Ross et al., 1977). The second hypothesis is "response to retention"; LDL is deposited in the intimal space and undergoes modification. Modified LDL serves as a chemoattractant for monocytes and macrophages. Macrophages remove modified LDL via scavenger receptors and become foamy (Williams and Tabas, 1995). In brief, LDL accumulates within the intimal space and subsequently undergoes modification such as oxidation,

Figure 1 Shows the atherosclerosis-plaque develops in the coronary arteries.