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Mini Review

Can BMP-1 Be a New Candidate Gene for CVD?

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Abstract

Cardiovascular diseases are quite common in the world as a cause of death and usually result in occlusion of the plaques of the arteries.

HDL is a very heterogeneous structure brought about by circulating small lipoproteins. The epidemiological studies also demonstrate the inverse relationship between HDLc levels and cardiovascular diseases. The twin studies have also indicated that the diversity of HDLc levels is 50% genetically based. Comprehensive literature studies show that there are 50 different genes associated with HDL.

Apo lipoprotein A1 is the major protein of HDL. It is secreted as proprotein and then cleaved by C-terminal procollagen endoproteinase / bone morphogenetic protein-1 (BMP-1).Studies carried out with recombinant BMP-1, BMP-1 antibody, and BMP-1 siRNA support that human hepatic (HepG2) cells and this proteinase, which is the only Apo A1-converting activity in the major secreted from CHO cells, stabilize ApoA1 expression. BMP-1 stimulates the conversion of the newly secreted phospholipid-linked priapo A1. Inhibition of BMP activity inhibits maturation of Apo A1.

Keywords: Cardiovascular diseases, BMP-1, Atherosclerosis, HDL

Introduction

Cardiovascular Diseases (CVD) are the most important cause of mortality and morbidity [1]. Hyperlipidemia and atherosclerosis are the most important causes of CVD. In developed countries, studies have been focused on controlling atherosclerosis and related diseases in recent years. Factors in the development of atherosclerosis can be changed and unchangeable risk factors are defined. Unmodifiable risk factors include age, gender, and genetic predisposition and the interchangeable factors are smoking, lifestyle and diet [2]. Hyperlipidemia, which is considered to be the most important risk factor for atherosclerosis, is characterized by a low concentration of Low Density Lipoprotein (LDL) -Cholesterol (LDL-C) and a low concentration of High Density Lipoprotein (HDL) -Cholesterol (HDL-C) [3]. The only lipoprotein that acts against the development of atherosclerotic diseases is HDL, which has antiatherogenic feature [4].

The main function of HDL is to carry the peripherally located cholesterol to the liver. Lecithin Cholesterol Acyl Transferase enzyme (LCAT) is required to take cholesterol from the periphery. This enzyme takes the fatty acid in the 2nd lecithin present in HDL and esterifies the free cholesterol. Thus, cholesterol gains hydrophobic property and is transported to the center of HDL [5]. The most important activator of the LCAT enzyme is Apo protein A1 (ApoA1), which is the main protein of HDL [6]. Despite the use of exercise and Statin therapy in the treatment of low HDL levels currently observed in hyperlipidemia, ApoA1 deficiency is examined in people without elevated HDL-C levels. The ApoA1 level is considered to be a more sensitive indicator of HDL-C following cholesterol metabolism. Molecular defects caused by mutations in the ApoA1 gene lead to the degradation of HDL synthesis and molecular function. It is necessary to trim the ApoA1 with "Bone Morphogenetic Protein (BMP)" to be able to mature. BMP-1 not only cleaves and activates the Apo A1 proprotein; it also increases the amount by reducing the clearance of this molecule [7]. All this information suggests that BMP-1 is directly involved in HDL metabolism.

BMP-1

BMP-1 (C-terminal procollagen endoproteinase-1; BMP1 / mammal tld) locates in chromosome 8. It is not one of the authentic BMP protein family members and belongs to the "astacin / BMP1 / Tolloid (TLD) -like family" of zinc metalloproteinases involved in the formation and development of the extracellular matrix. BMP-like proteases commonly have an amino-terminal prod rug structure that is cleaved for mature protease efficiency [8]. Mature BMP1; three complement dominant (CUB) proteins are thought to be the Epidermal Growth Factor (EGF) –like motifs following the metalloprotease domain and protein-protein interactions.

ApoA1 has not previously been identified as a BMP-1 substrate. However, it is known that the renal kubulin protein, which has 27 CUB domains, binds to lipid-poor ApoA1 and stimulates its recycling [9].

BMP-1 encodes the conversion of pro-ApoA1 to its phospholipid-binding form, thus promoting functional HDL formation and reverse cholesterol transport. A2-macroglobulin, a protease inhibitor secreted as an immune response, blocks proApoA1 maturation by inhibiting BMP-1 activity. It is proposed that the α2-macroglobulin-BMP-1 mediated characteristic response may be responsible for the reduction of ApoA1 levels that occur in inflammation or infection [10].

Phuonglan Chau et al. reported in 2007 that stimulating the conversion of pro Apo A1 to its phospholipid-binding form is the only effect of BMP-1, which has the CUB domain, such as the kubulin

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protein [7]. This need to be supported with more work but it is a very valuable and exploratory issue in terms of atherosclerosis which is a very big risk factor for CHD.

Conclusion

As a result, cardiovascular diseases are a very important health problem. Therefore, the identification of candidate genes that predispose to cardiovascular diseases is very important. For this reason, BMP-1 is a new and exploratory subject.

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