Mini Review

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

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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 endopeptidase-1; BMP1 / mammal tld) locates in chromosome 8. It is not one of the authentic BMP family members and belongs to the “astacin / BMP1 / Tolloid (TLD) -like family” of zinc metallopeptidases involved in the formation and development of the extracellular matrix. BMP-like proteases commonly have an amino-terminal propeptide 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 a2-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 proteinase. This property is a potential therapeutic strategy for HDL metabolism.
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.

**References**

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